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

Xuping Song, Yue Hu, Yan Ma, Liangzhen Jiang, Xinyi Wang, Anchen Shi, 3 Junxian Zhao, ¹ Yunxu Liu, ¹ Yafei Liu, ¹ Jing Tang, ¹ Xiayang Li, ¹ Xiaoling Zhang ⁶, ⁴ Yong Guo, ⁵ Shigong Wang⁴

To cite: Song X, Hu Y, Ma Y, et al. 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. BMJ Open 2022;12:e049516. doi:10.1136/ bmjopen-2021-049516

Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/ bmjopen-2021-049516).

Received 29 January 2021 Accepted 31 March 2022



@ Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by

For numbered affiliations see end of article.

Correspondence to

Professor Xiaoling Zhang; xlzhang@ium.cn and Professor Shigong Wang; wangsg@cuit.edu.cn

ABSTRACT

Objective Adverse health effects of fine particles (particulate matter, s) 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 (1) to explored the effects of BC and EC on cardiovascular and respiratory morbidity and mortality, and (2) to verified the reliability of the metaanalysis 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 19 July 2021.

Eligibility criteria for selecting studies Time series, case cross-over 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 analysed via a random effects model and reported as relative risk (RR) with 95% Cl. The certainty of evidences was assessed by adapted GRADE. The reliabilities of meta-analyses were analysed by p value plots.

Results Seventy studies met our inclusion criteria. (1) Short-term exposure to BC/EC was associated with 1.6% (95% CI 0.4% to 2.8%) increase in cardiovascular diseases per 1 µg/m³ in the elderly; (2) Long-term exposure to BC/EC was associated with 6.8% (95% CI 0.4% to 13.5%) increase in cardiovascular diseases and (3) 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 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.
- ⇒ This study incorporated a detailed search strategy, explicit literature screening and risk of bias assessment.
- ⇒ The p value plots were used to evaluate the reliabilities of meta-analyses.
- Limitation on searching grey literature should be noted.

BACKGROUND

Black carbon (BC), a ubiquitous component of air particulate matter (PM), is usually measured through optical absorption.¹ Elemental carbon (EC), another carbonaceous material with a graphitic structure, is commonly measured by thermal or thermooptical method.^{1 2} Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustionrelated sources and is a measured component of the PM. The adverse health effects of PM, especially PM_{9.5}, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.3-5 PM_{9.5} is composed of various constituents, in which some of them are more toxic and hypothesised as the main cause of the adverse effects of PM_{9.5}. 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. 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. 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 analysed the impact of BC on health. Nevertheless, quantitative associations between BC exposure and cardiovascular and respiratory diseases have not been well-characterised due to different objectives of the reviews. ¹⁷ ¹⁸ A series of eligible studies published recently have not been considered. In addition, the GRADE (Grading of Recommendations assessment, Development and Evaluation) framework was not adopted in previous systematic reviews. Compared with Yang et al, 19 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 shortterm and long-term exposure to BC/EC with the respiratory and cardiovascular morbidity and mortality; and (2) to verify the reliability of the meta-analysis using p value plots.

METHODS

Patient and public involvement

Patients or the public were not involved in this study.

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 19 July 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 online supplemental table S1.

Inclusion and exclusion criteria

A time series study, case cross-over 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 cross-over 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 (ICD9 codes 460-519, 786.07, 786.09 or 162; ICD-10 codes [00–[99, R06.251, R06.001 or C34) or cardiovascular diseases (ICD9 codes 390–459, ICD-10 codes I00–I99); (4) studies considering morbidity or mortality as outcome; (5) estimates were OR, relative risk (RR) or HR with 95% CI or enough information for their calculation and (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 (eg, chronic obstructive pulmonary disease (COPD) and asthma); (3) studies focusing on particular populations (eg, pregnant women and miners) or population living in specific environments with high pollution concentration (eg, residential area near industrial complexes, population exposed to sugar cane burning and neighbourhoods that expose many streets); (4) studies focusing on seasonality; (5) conference abstracts and (6) study period less than 1 year.

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 standardised 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.

Data synthesis

Regarding the meta-analysis, the RR was used as an effect estimate, and the OR in case cross-over 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 standardised increment (1 $\mu g/m^3$) of RR. The following formula was used to calculate standardised risk estimates:

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

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 analysed in different studies and the latest study was included. ^{24–26}

Risk of bias assessment

The risk of bias was assessed for each study according to the Office of Health Assessment and Translation 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.

Evaluation of certainty of evidence

An adaptation of the GRADE framework, formulated by the WHO 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; three reasons were used to upgrade: large magnitude of effect size, all plausible confounding shifts the RR towards the null and concentration-response gradient. To evaluate the magnitude of the effect size, the E-value was calculated using the following formula:

$$E - value = RR + sqrt \{RR * (RR - 1)\}$$

Statistical analysis

Statistical analysis was performed using STATA (V.12.0, Stata Corp). In this meta-analysis, the random-effects model was conducted for anticipating significant heterogeneity among studies. Heterogeneity among trials was assessed by the χ^2 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_{9.5} 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_{9.5}-unadjusted estimates in the models were combined, respectively where more than three estimates were available. Regarding the subgroup analysis, PM_{9 5}-unadjusted estimates were analysed, while PM_{9 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 analysed and presented results of cardiovascular or respiratory diseases, hence systematic diseases were analysed 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. A 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. Fifteen 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 and Kindzierski. 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° 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:

$$SE = \left(\ln CI \text{ high} - \ln CI \text{ low}\right) / 2 / 1.96$$

$$Z = \ln RR / SE$$

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

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 analysed 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 cross-over 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 analysed both cardiovascular and respiratory diseases, 18 studies merely investigated cardiovascular diseases, and 17 studies assessed respiratory diseases. Thirty-seven studies were conducted in the USA, 14 in China, 4 in Canada, 2 in the UK, Sweden, Korea and Serbia, 1 in Denmark, Iran, Germany and the Netherlands. The remaining three studies collected data from two different countries: Spain and Greece, Spain and Italy, Sweden and Denmark. Twenty-seven studies

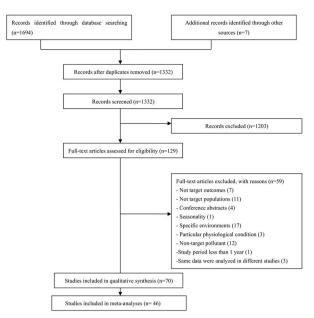


Figure 1 Flow diagram of hliterature screening process.

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 seven studies did not employ the ICD standards (online supplemental table S2). In addition, the authors of 33 studies were contacted, but only 19 answered our request (response rate: 57.6%).

Short-term effect of BC/EC on cardiovascular and respiratory diseases

Overall, short-term exposure to BC/EC was associated with an increased risk of cardiovascular diseases (RR 1.007 per $1 \mu g/m^3$, 95% CI 1.002 to 1.011) (adjusted by trim and fill method) in overall analyses (table 1 and figure 2). Cardiovascular diseases (RR 1.016 per $1 \mu g/m^3$, 95% CI 1.004 to 1.028) were associated with BC/EC in the elderly (65+ years) (figure 2).

Impact of BC/EC on cardiovascular diseases was related to the exposure lag. The estimates of the association were strongest on the day of the event (lag 0) (RR 1.011 per $1 \mu g/m3$, 95% CI 1.006 to 1.016), and then diminished on lag 1 (RR 1.005 per 1 μ g/m³, 95% CI 1.002 to 1.008) and lag 2 (RR 1.002 per 1 μ g/m³, 95% CI 0.999 to 1.005) (online supplemental 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 to 1.005). However, no association was found in America (RR 1.017, 95% CI 0.998 to 1.037) and Europe (RR $0.990,\,95\%$ CI 0.979 to1.001) (online supplemental figure S1). On the other hand, an increased risk of cardiovascular morbidity was observed in America (RR 1.022, 95% CI 1.016 to 1.029) with short-term exposure to BC/EC, while only one study performed in Europe (RR 1.026, 95% CI 1.006 to 1.047) investigated the short-term effect of BC/EC on cardiovascular morbidity.²³ In addition, just one study in Asia

	PM _{2.5} -una	PM _{2.5} -unadjusted model				PM _{2.5} -adju	PM _{2.5} -adjusted model		
Subgroup analysis	No of studies	No of estimates	Relative Risk (95% CI)	2	Egger regression test (p value)	No of studies	No of estimates	Relative Risk (95% CI)	12
Cardiovascular diseases	ses								
Age									
All population	20	22	1.008 (1.004 to 1.012)	64.40%	0.007	9	7	1.014 (1.001 to 1.027)	51.00%
Relative risk adjusted for publication bias with trim and fill method	24	26	1.007 (1.002 to 1.011)	I	1	L	I	I	I
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	91	1.006 (1.002 to 1.010)	%00.09	0.020	1	T	I	1
≥65 years	5	9	1.016 (1.004 to 1.028)	87.40%	I	Ι	I	ı	I
Outcome									
Morbidity	12	12	1.022 (1.016 to 1.029)	37.20%	0.163	4	5	1.018 (1.006 to 1.031)	39.50%
Mortality	41	15	1.003 (1.001 to 1.006)	29.70%	0.266	4	4	1.006 (0.993 to 1.019)	42.90%
Respiratory diseases									
Age									
All population	16	18	1.010 (0.996 to 1.025)	87.20%	0.627	2	8	1.002 (0.990 to 1.014)	43.80%
Sensitive analysis on study of partial temporal overlap from the same geographical location	12	12	1.008 (0.992 to 1.023)	%08.06	0.449	1	I	I	1
>65	က	4	1.038 (1.006 to 1.071)	82.90%	1	1	I	ı	1
Outcome									
Morbidity	10	10	1.012 (0.993 to 1.031)	91.80%	0.671	က	2	0.996 (0.987 to 1.004)	0
Mortality	10	1	1.013 (0.997 to 1.030)	66.40%	0.328	က	က	1.017 (0.985 to 1.050)	48.30%

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.

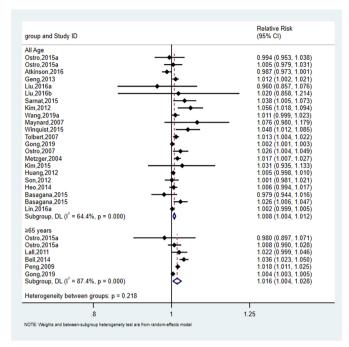


Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM_{2.5}-unadjusted model. BC/EC, black carbon/elemental carbon; PM, particulate matter.

performed the short-term effects of BC/EC on stroke morbidity (online supplemental figure S2).⁶⁶

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

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

We chose at random 15 studies included in the metaanalysis. Then, we extracted analysis items (outcomes, predictors, covariates, and lags) and calculated the search spaces. Table 2 lists 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 online supplemental table S4. Across the studies, the median number of possible analyses was 12 000 (IQR 2688–15 360) 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 9 p values less than 0.05 and 13 larger than 0.05 (online supplemental 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° line. Four calculated p values were less than 0.05, while 14 were larger than 0.05 and fell on an approximate 45° line (online supplemental 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°, the impact of short-term exposure to BC/EC on respiratory diseases was likely to be random.

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 to 1.135) (online supplemental figure S3). Three studies assessed the long-term exposure to BC/EC and ischaemic heart disease (IHD), and a positive association was observed (RR 1.066,

Table 2	Variable counts and anal	ysis search spa	aces for the 15	studies chosen	from the	meta-analys	is	
No	Study	Outcome	Predictor	Covariate	Lag	Space1	Space2	Space3
1	Atkinson, 2016 ⁹³	3	7	6	2	42	64	2688
2	Geng, 2013 ⁴⁹	3	1	5	3	9	32	288
3	Sarnat, 2015 ⁵⁹	8	22	5	4	704	32	22 528
4	Kim, 2012 ⁹⁴	3	5	6	15	225	64	14 400
5	Maynard, 2007 ⁷⁹	4	2	5	1	8	32	256
6	Winquist, 2015 ⁶³	4	8	6	3	96	64	6144
7	Gong, 2019 ⁴²	1	2	7	9	18	128	2304
8	Huang, 2012 ⁸⁷	3	13	6	7	273	64	17 472
9	Basagaña, 2015 ²³	5	16	6	3	240	64	15 360
10	Son, 2012 ⁴⁷	3	11	5	7	231	32	7392
11	Heo, 2014 ⁵⁷	3	9	7	4	108	128	13 824
12	Kim, 2015 ⁸⁸	5	5	5	15	375	32	12 000
13	Tolbert, 2007 ⁸⁰	2	13	7	3	78	128	9984
14	Wang, 2019a ⁴⁶	3	6	6	11	198	64	12 672
15	Metzger, 2004 ³⁸	6	14	5	8	672	32	21 504

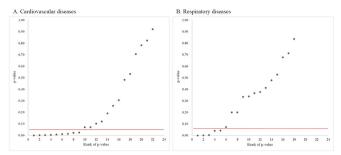


Figure 3 P value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the PM_{2.5}-unadjusted model. BC/EC, black carbon/elemental carbon; PM, particulate matter.

95% CI 1.009 to 1.127). On the other hand, four 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 analysed COPD. It indicated that long-term exposure to BC/EC was associated with an increased risk of COPD morbidity (RR 1.060, 95% CI 1.020 to 1.100), while no impact was observed for COPD mortality (RR 1.070, 95% CI 1.000 to 1.140).²⁴

Results from the $PM_{2.5}$ -adjusted model

In the PM_{9.5}-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 μg/m³, 95% CI 1.001 to 1.027) (online supplemental figure S4). The meta-analysis indicated that the association was robust compared with the results of the PM_{9.5}-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the PM_{9.5}-adjusted model (RR 1.018 per 1 $\mu g/m^3$, 95% CI 1.006 to 1.031) was consistent with the results in the PM_{9.5}-unadjusted model (RR 1.022 per 1 µg/ m³, 95% CI 1.016 to 1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the PM_g-unadjusted model (RR 1.003 per 1 µg/m³ 95% CI 1.001 to 1.006), while no association was observed in the PM_{0.5}-adjusted model (RR 1.006 per 1 µg/m³, 95% CI 0.993 to 1.019) (table 1).

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 to 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 µg/m³, 95% CI 0.992 to 1.023) between respiratory diseases and BC/ EC after eliminating overlapped studies (table 1). 21 23 88 94

Risk of bias and certainty of evidence

The risk of bias assessment of the included studies is shown in online supplemental table S6 and more analytically in online supplemental 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, seven 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 9

The certainty of evidence on the acute effects of BC/ EC on cardiovascular diseases in the PM_{9 E}-adjusted model was rated as 'moderate' and in the PM_{9 x}-unadjusted model was rated as 'low'. The evidence on the chronic effects of BC/EC on cardiovascular diseases was evaluated as 'moderate' certainty (online supplemental table S8).

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.

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_{9.5}-adjusted model and the PM_{9.5}-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 online supplemental table S4 indicates that small p values could be the result of multiple testing/multiple modelling.

However, the association between BC/EC and cardiovascular mortality should be further explored by further studies, which should pay more attention to the PM_{9.5}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_{9.5}-unadjusted model and PM_{9.5}-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 PM_{9 5}-adjusted model, no statistically significant difference was observed between EC (RR 1.039, 95% CI 0.993 to 1.083) and cardiovascular morbidity. In addition, Samoli et al illustrated that the impact of BC/EC on cardiovascular morbidity differed in the elderly and other age groups, while Atkinson et al indicated no statistically significant difference between BC/EC and cardiovascular mortality in both the PM_{9.5}adjusted model and PM_{9,5}-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.

Vulnerable populations

This meta-analysis revealed that BC/EC may have acute effects on cardiovascular diseases in the elderly. 100 In addition, lung function and mucociliary clearance decline with long-term exposure to pollutants and increasing age. $^{5\ 101}$ 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 $_{2.5}$.

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 repolarisation 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.* ¹⁰⁵ A critique was given in Stanley Young and Kindzierski who used p value plots to call those claims into question. ³⁰

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 cross-over studies, especially for influenza epidemics. Influenza epidemics are factors usually neglected in shortterm studies. Second, studies should adjust PM_{9.5} when assessing the health effect of PM_{9.5} constituents. Mostofsky et al showed that PM_{9.5} may be associated with both health and its constituents. Constituents having closer association with PM95 may illustrate a stronger association with diseases. Therefore, the results of PM_{9 s}-unadjusted model could introduce bias. 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.

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 modelling 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 three estimates. Most of the included papers used in our study were from the USA 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 analysed 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.

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.

Author affiliations

¹School of Public Health, Lanzhou University, Lanzhou, Gansu, China

Acknowledgements We would like to thank the authors of the original studies for their contributions to our systematic review and meta-analysis, especially authors who provided their raw data for the analysis. We are grateful to Professor S. Stanley Young and all reviewers for their helpful comments and suggestions on this manuscript. We would like to thank MogoEdit company for helping us in the language editing of our article.

Contributors SW, XZ and XS developed the research design. XS, YH, YM and LJ analysed 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. XS is the guarantor and accepts full responsibility for the work

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

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID ID

Xiaoling Zhang http://orcid.org/0000-0003-0434-1286

REFERENCES

- 1 Bond TC, Doherty SJ, Fahey DW, et al. Bounding the role of black carbon in the climate system: a scientific assessment. J Geophys Bes 2013:118:5380–552
- 2 Zencak Z, Elmquist M, Gustafsson Örjan. Quantification and radiocarbon source apportionment of black carbon in atmospheric aerosols using the CTO-375 method. *Atmos Environ* 2007;41:7895–906.
- 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;69:660–5.
- 4 GBD 2017 Risk Factor Collaborators. 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;392:1923–94.
- 5 Ross MA. Integrated science assessment for particulate matter. Washington DC, USA: US Environmental Protection Agency, 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;115:989–95.
- 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;176:317–26.
- 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. Copenhagen, Denmark: for Europe, 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;64:620–60.
- 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;289:573–88.
- 1 Colicino E, Giuliano G, Power MC, et al. Long-Term exposure to black carbon, cognition and single nucleotide polymorphisms

²Second Clinical College, Lanzhou University, Lanzhou, Gansu, China

³Department of General Surgery, Xi'an Jiaotong University Medical College First Affiliated Hospital, Xi'an, Shaanxi, China

⁴College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu, Sichuan, China

⁵Department of Civil Affairs in Guizhou Province, Guizhou Province People's Government, Guiyang, Guizhou, China



- in microRNA processing genes in older men. *Environ Int* 2016;88:86–93.
- 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;48:8–16.
- 13 Young SS. Air quality environmental epidemiology studies are unreliable. Regul Toxicol Pharmacol 2017;86:177–80.
- 14 Simonsohn U, Nelson LD, Simmons JP. p-Curve and effect size: correcting for publication bias using only significant results. *Perspect Psychol Sci* 2014;9:666–81.
- 15 Spellman BA. The seven deadly SINS of psychology: a manifesto for reforming the culture of scientific practice. *Nature* 2017;544:414–5.
- 16 Munafo M. Rigor mortis: how sloppy science creates Worthless cures, Crushes hope, and wastes Billions. NATURE 2017:543:619–20.
- 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;109:89–100.
- 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. Environ Pollut 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;70:458–66.
- 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;123:549–56.
- 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;73:300–7.
- 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;187:721–7.
- 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;72:123–9.
- 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;124:785–94.
- 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, 2015. https://ntpniehsnihgov/ntp/ohat/ pubs/ handbookjan2015 508pdf
- 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: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. Crit Rev Toxicol 2019;49:85–94.
- 31 Schweder T, Spjotvoll E. Plots of *P* -values to evaluate many tests simultaneously. *Biometrika* 1982;69:493–502.
- 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;38:905–12.
- 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.
- 6 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;180:968–77.
- 87 Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. J Epidemiol Community Health 2006;60:890–5.
- 38 Metzger KB, Tolbert PE, Klein M, et al. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology* 2004;15:46–56.
- 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;71:129–36.
- 40 Mar TF, Norris GA, Koenig JQ, et al. Associations between air pollution and mortality in Phoenix, 1995-1997. Environ Health Perspect 2000:108:347–53.
- 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;125:97–103.
- 42 Gong T, Sun Z, Zhang X, et al. Associations of black carbon and PM2.5 with daily cardiovascular mortality in Beijing, China. Atmos Environ 2019;214:116876.
- 43 Wang Y, Shi Z, Shen F, et al. Associations of daily mortality with short-term exposure to PM_{2.5} 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 timeseries analysis. *Environ Health Perspect* 2014;122:837–42.
- 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 ≥ 65 years of age. Environ Health Perspect 2014;122:138–44.
- 46 Wang M, Hopke PK, Masiol M, et al. Changes in triggering of STelevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study. Environ Health 2019;18:82.
- 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;120:872–8.
- 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;64:148–55.
- 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;219:204–11.
- 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;119:455–60.
- 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;115:13–19.
- 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;117:475–80.
- 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;117:957–63.
- 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 casecrossover study. *Medicina* 2019;55:261.
- 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;25:379–88.
- 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;123:437–44.
- 60 Lavigne Éric, 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;120:373–8.
- 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;119:467–73.
- 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;25:215–21.
- 64 Ostro BD, Feng W-Y, Broadwin R, et al. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. Occup Environ Med 2008;65:750–6.
- 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;61:1281–91.
- 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;10:446–60.
- 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;117:99–106.
- 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 2020:142:105854.
- 71 Liu L, Zhang Y, Yang Z, et al. Long-Term exposure to fine particulate constituents and cardiovascular diseases in Chinese adults. J Hazard Mater 2021;416:126051.
- 72 Liu S, Jørgensen 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;146:106267.
- 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;127:107012.
- 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;119:501–7.
- 75 Hvidtfeldt UA, Sørensen M, Geels C, et al. Long-term residential exposure to PM_{2.5}, 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 timeseries analysis of the differential toxicity of major fine particulate matter constituents. Am J Epidemiol 2012;175:1091–9.
- 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;25:843–50.
- 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;115:751–5.
- 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:S29–35.
- 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. 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. Boston, MA: Res Rep Health Eff Inst, Health Effects Institute, 2013.

- 83 Lin H, Tao J, Du Y, et al. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. Environ Pollut 2016;208:758–66.
- 84 Jung C-R, Young L-H, Hsu H-T, et al. PM_{2.5} components and outpatient visits for asthma: A time-stratified case-crossover study in a suburban area. *Environ Pollut* 2017;231:1085–92.
- 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. J Environ Health Sci Eng 2021;19:907–16.
- 86 de Kluizenaar Y, van Lenthe FJ, Visschedijk AJH, et al. Road traffic noise, air pollution components and cardiovascular events. Noise Health 2013;15:388–97.
- 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;175:556–66.
- 88 Kim S-Y, Dutton SJ, Sheppard L, et al. The short-term association of selected components of fine particulate matter and mortality in the Denver aerosol sources and health (DASH) study. Environ Health 2015:14:49
- 89 Strickland MJ, Darrow LA, Klein M, et al. Short-Term associations between ambient air pollutants and pediatric asthma emergency department visits. Am J Respir Crit Care Med 2010;182:307–16.
- 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. Atmos Environ 2016;147:369–75.
- 91 Kovačević G, Tomić-Spirić V, Marinković J, et al. Short-Term effects of air pollution on exacerbations of allergic asthma in Užice region, Serbia. Postepy Dermatol Alergol 2020;37:377–83.
- 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;121:1148–53.
- 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;26:125–32.
- 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;120:1094–9.
- 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;119:461–6.
- 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;60:163–75.
- 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;28:1397–408.
- 98 Chen P, Kang S, Gul C, et al. Seasonality of carbonaceous aerosol composition and light absorption properties in Karachi, Pakistan. J Environ Sci 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;178:865–76.
- 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 agematched healthy controls: a randomised, crossover study. Lancet 2018;391:339–49.
- 102 Phalen RF, Oldham MJ, Kleinman MT. TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS. In: Dodgson J, McCallum RI, Bailey MR, et al, eds. Inhaled particles VI: Pergamon, 1988: 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;71:1157–61.
- 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;113:440–6.
- 105 Mustafic H, Jabre P, Caussin C, et al. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. JAMA 2012;307:713–21.

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^c, Shigong Wang*^b

Corresponding author 1:

Name: Xiaoling Zhang

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

Technology, Chengdu 610000, Sichuan, China

E-mail address: xlzhang@ium.cn

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

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

Technology, Chengdu 610000, Sichuan, China

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

Fax: 028-85966502

^a School of Public Health, Lanzhou University, Lanzhou 730000, China;

^b College of Atmospheric Sciences, Chengdu University of Information Technology, Chengdu 610000, China;

^c Second Clinical College, Lanzhou University, Lanzhou 730000, China;

^d Department of General Surgery, The First Affiliated Hospital of Xi'an Jiao Tong University, Shaanxi 710061, China;

^e Department of Civil Affairs in Guizhou Province, Guiyang 550004, China.

Supplementary data

- Table S1 Search strategy in PubMed.
- **Table S2** Characteristics of the included studies in the systematic review and meta-analysis.
- **Table S3** Subgroup analysis on short-term effects of BC/EC on cardiovascular and respiratory diseases.
- **Table S4** Summary statistics for the number of possible analyses using the three search spaces.
- **Table S5** The p-value calculation process for each study using RR, CI low and CI high.
- Table S6 Results of risk of bias assessment.
- Table S7 Details of risk of bias assessment.
- **Table S8** Assessment of certainty of evidence for the outcomes.
- **Figure S1** Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.
- **Figure S2** Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.
- Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.
- **Figure S4** Impact of short-term exposure to BC/EC on cardiovascular diseases in the PM_{2.5}-adjusted model.

Table S1 Search Strategy for PubMed.

No.	Search Strategy
#1	particulate matter/or aerosols.sh.
#2	particulate matter*/or "PM10"/or "PM2.5"/or fine particle*/or thoracic particle*/or ultrafine/or aerosol*/or carbon*/or soot*.ti,ab.
#3	"PM".tw.
#4	or/1,2,3
#5	"EC" /or "BC".tw.
#6	and/4,5
#7	black carbon*/or elemental carbon*/or element carbon*.ti,ab.
#8	or/6,7
#9	respiratory tract disease.sh.
#10	respirat*/or pulmonary disease*/or lung/or chest infection*/or airway/or asthma*/or pneumonia*/or "chronic obstructive pulmonary disease"/or COPD.ti,ab.
#11	cardiovascular diseases.sh.
#12	cardio*/or cardiop*/or cardior*/or heart/or coronary/or vascular/or blood/or cardiac.ti,ab.
#13	or/9,10,11,12
#14	morbidity/or hospitalization/or death/or mortality/or outpatient.sh
#15	morbidit*/or hospitalisation*/or hospitalization*/or death*/or mortalit*/or outpatien*/or emergency room*/or emergency department*/or emergency admi*/or hospital
π13	admission*.ti,ab.
#16	or/14,15
#17	epidemiologic studies/or cross over study.sh.
#18	time series*/or timeseries*/or case cross*/or casecross*.tw.
	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag non-linear model/or distributed lag non-linear
#19	model/or distributed lag model/or quasipoisson*/or poisson*/or generalized estimating equation/or generalised estimating equation/or GAM/or GLM/or DLNM/or GEE/or DLM/or
	ARIMA.tw.
#20	cohort*/or follow up*/or observational/or longitudinal/or case control*/or epidemiologic/or population
#20	stud*/or prospective*/or retrospective*.tw.
#21	or/17,18,19,20
#22	and/8,13,16,21

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

64.1	Study	G .	Study	0.4		D.H. c	ICD	D.
Study	Design	Country	Period	Outcome	Age	Pollutant	code	Diseases
Atkinson et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
								RES[COPD(ICD-9-CM:490-492,RTI(ICD-9-CM:464-466, 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 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	Asthma(ICD-10:J45)
Geng et al. 2013	TS	China	2007-2008	Mortality	All	ВС	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
			2008-2009					
0 1 2015	CC.	Spain,	(Athens),	N6 - 12	A 11	D.C.	ICD 10	CUDICD 14 144 144 PEC/CD 14 144 144
Ostro et al. 2015a	CS	Greece	2009-2010(Barc	Mortality	All	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
			elona)					
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all	BC,EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99)
Samon et al. 2010	13	UK	2011-2012	Worblatty	(RES)	вс,ес	ICD-10	CVD(ICD-10.100-197), RE3(ICD-10.300-397)
Zanobetti and Schwartz	CS	USA	1995-1999	Morbidity	≥65	ВС	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480-487)
2006	CS	CDA	1,,,,,	Wording		ВС	icb)	111(100). 110), i icumolina (100). 100 (01)
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(ICD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(I
20104	15	05.1	2000 2013	Morelany			105 /	CD-9:480-486),Asthma(ICD-9:493),SSID(ICD-9:780-799)
Liu et al. 2016b	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RESP(ICD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia
20100	.5	05.1	2000 2013	Morelany	- 	20	ieb,	(ICD-9:480-486),Asthma(ICD-9:493)
								CVD[IHD(ICD9:410-414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	(ICD9:433-437,440,443-445,451-453)],RES[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)

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

Study	Study	Country	Study	Outcome	Ago	Pollutant	ICD	Diseases
Study	Design	Country	Period	Outcome	Age	ronutant	code	Diseases
Ostro et al. 2009	TS	USA	2000-2003	Morbidity	<19	EC	ICD9	RES(ICD-9:460-519), Asthma(ICD-9:493), Acute bronchitis(ICD-9:466), Pneumonia(ICD-9:480-486)
Kim et al. 2015	TS	USA	2003-2007	Mortality	All	EC	ICD-10	CVD,RES
Huang et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	RES(ICD-10:100-198),CVD(ICD-10:100-199)
								CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhythm 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-9:490-492),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 480-487).
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)
D	CS	C I4-1	2003-2013	Morbidity,	All	EC	ICD-9,	CVD/ICD 0.200 450 ICD 10.100 IO0 DEC/ICD 0.470 510 ICD 10.100 IO0)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Mortality	All	EC	ICD-10	CVD(ICD-9:390-459,ICD-10:I00-199),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: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-10:100-199)
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-10:101-199),RES(ICD-10:J00-J99)
								RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477,480-486,491,492,493,496,786.07),CVD(ICD-9:410-414,427,
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	428,433-437,440,443-445,451-453)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J98)
T. H 1 2000	TO	TIG A	1000 2000	M 1175	4.11	EG	ICD 0	CVD(ICD-9:402,410-414,427,428,433-437,440,444,451-453),RES(ICD-9:460-466,477,480-486,491,492,493,496,
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	786.09)

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

Ct. 1	Study	G .	Study	0.4		D.H. c.	ICD	n:
Study	Design	Country	Period	Outcome	Age	Pollutant	code	Diseases
Wang and Lin 2016	TS	China	2004-2010	Morbidity, Mortality	≥65(mortality), all(morbidity)	EC	ICD-9	CVD(ICD-9-CM:390-459),RES(ICD-9-CM:460-519)
Darrow et al. 2014	TS	USA	1993-2010	Morbidity	0–4	EC	ICD-9	Acute Bronchitis or Bronchiolitis(ICD-9:466),Pneumonia(ICD-9:480-486),URI(ICD-9:460-465)
Metzger et al. 2004	TS	USA	1993-2000	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),AMI(ICD-9:410),cardiac 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(ICD-9:440),Stroke(ICD-9:436)]
Mar et al. 2000	TS	USA	1995-1997	Mortality	All	EC	ICD-9	CVD(ICD-9:390-448.9)
Wang et al. 2019a	TS	China	2013-2015	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
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)
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-I22),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-10:160-169)]
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagic Stroke(ICD-9:430-432)]
Tomic'-Spiric' et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	ВС	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)]
Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	ВС	ICD-9, ICD-10	CVD(ICD-9:390-429,ICD-10:I01-I52),Stroke(ICD-9:430-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD-10:J00-J99)
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	Asthma,URTI,LRTI
Krall et al. 2013	TS	USA	2000-2005	Mortality	All	EC	NR	CVD and RES(NR)
Cakmak et al. 2009	TS	Canada	2001-2006	Morbidity	All	EC	ICD-9	RES(ICD-9:460-519)

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

Gr. 1	Study	G	Study	0.4		D.II.	ICD	D:
Study	Design	Country	Period	Outcome	Age	Pollutant	code	Diseases
								CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(ICD-9:427),CHF(ICD-9:428),PVD and Cerebrovascular
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	Events(ICD-9:433-437,440,443-445,451-453)],
Tolocit et al. 2007	13	USA	1993-2004	Worbidity	All	EC	ICD-9	RES[Asthma(ICD-9:493,786.07,786.09), COPD(ICD-9:491,492,496), URTI(ICD-9:460-465,460.0,477), Pneumonia, Particular (ICD-9:493,786.07), Pneumonia, Pneum
								(ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
								RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490-492,496),Acute Bronchitis and
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	Bronchiolitis (ICD-9:466), Asthma (ICD-9:493)], CVD [Dysrhythmia (ICD-9:427), IHD (ICD-9:410-414), HF (ICD-9:410-414)], CVD [Dysrhythmia (ICD-9:427), IHD (ICD-9:410-414), IHF (ICD-9:410-414)], CVD [Dysrhythmia (ICD-9:410-414), IHF (ICD-9:410-414)], CVD [Dysrhythmia (ICD-9:427), IHD (ICD-9:410-414)], CVD [Dysrhythmia (ICD-9:410-414)], CV
								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		CVD(ICD-10:100-199)
				•			ICD-10	
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	BC	NO	Acute Ischemic Stroke
			1999-2009(Atlan					
			ta,Georgia),					
			2004-010(Birmi					
Krall et al. 2017	TS	USA	ngham,Alabama,	Morbidity	All	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:491,492,496),URTI(ICD-9:460-465,466.0,477),Asthma and/or
			2001-2007(St.Lo					Wheeze(ICD-9:493,786.07)]
			uis, Missouri),					
			2006-2009(Dalla					
0.7		***	s,Texas)	V 118	5.10	F.C.	YOR O	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
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),ARI(ICD-9:460.0-466.0)

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

C4 J	Study	Ct	Study	0	A	Pollutant	ICD	Diseases
Study	Design	Country	Period	Outcome	Age	Ponutant	code	Diseases
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,	all (mortality),	EC	ICD-9,	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
110 et al. 2013	13	USA	2001-2000	Mortality	≥65(morbidity)	EC	ICD-10	CVD(ICD-10.101-177), XES(ICD-10.300-377)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:100-199),IHD(ICD-10:120-125),Pulmonary(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)
Gair et al. 2013		Cunada	1777 2002	Mortality	15 05	ВС	ICD-10	COLD(ICD 7.734 172,170,RCD10.310 T1)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 –64	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J99,C34)
Thurston et al. 2016	Co	USA	1988-2004	Mortality	≥30	EC	ICD-9,	IHD(ICD-9:410-414,ICD-10:120-125)
							ICD-10	(/,,
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:100-199),RES(ICD-10:J00-J47,J80-J99)
Gan et al. 2011	Co	Canada	1999-2002	Morbidity,	45–85	ВС	ICD-9,	CHD(ICD-9:410-414,429.2),(ICD-10:I20-I25)
				Mortality			ICD-10	
De Kluizenaar et al.	Co	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
2013								
Vedal et al. 2013	Co	USA	1994-2005	Morbidity,	50-79	EC	ICD-9	CVD (ICD-9:CM 410-452)
				Mortality				
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(ICD 10:I20-I25)
Liu et al. 2021b	Co	China	2010–2017	Morbidity	All	BC	NR	CVD(including but not limited to hypertension and stroke)
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
Kovačević et al. 2020	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	AA(ICD-10:J45.0) or asthma with coexisting AR
Hasslöf et al. 2020	Со	Sweden	1991-1994	Morbidity	All	BC	NR	Atherosclerosis in the carotid arteries

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

Charles	Study	Ct	Study	0	A =	D-II44	ICD	Di
Study	Design	Country	Period	Outcome	Age	Pollutant	code	Diseases
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI
Ljungman et al. 2019	Co	Sweden	1990-2011	Morbidity,	All	ВС	ICD-9,	IHD(ICD-9:410–414 and ICD-10:120-25);stroke(ICD-9:431–436 and ICD-10:161–165)
Ljungman et al. 2019	Co	Sweden	1990-2011	Mortality	All	ьс	ICD-10	ImD(ICD-9.410-414 and ICD-10.120-23), stroke(ICD-9.451-450 and ICD-10.101-103)
Liu et al. 2021a	Co	Sweden,	1992-2004	Morbidity	All	ВС	ICD-9,	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40–44)
Liu et al. 2021a	Co	Denmark	1992-2004	Moroidity	All	ВС	ICD-10	COTD(ICD-5.470-452, alid 474-450, of ICD-10.340-44)

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

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

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

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

Table S4 Summary statistics for the number of possible analyses using the three search spaces.

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

Table S5 The p-value calculation process for each study using RR, CI low and CI high.

	Number	Study ID	RR	CI low	CI high	lnRR	lnCI low	lnCI high	SE	Z	p-values
	1	Ostro,2015a	0.994000	0.953000	1.038000	0.006018	0.048140	0.037296	0.021795	0.276122	0.782454
	2	Ostro,2015a	1.005000	0.979000	1.031000	0.004988	0.021224	0.030529	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	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
Cardiovascular Diseases	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	0.017768	2.638621	0.008324
Car diovascular Discuses	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	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	0.048999	0.623052	0.533250
	17	Huang,2012	1.005000	0.998000	1.010000	0.004988	0.002002	0.009950	0.003049	1.635761	0.101890
	18	Son,2012	1.001000	0.981000	1.021000	0.001000	0.019183	0.020783	0.010195	0.098036	0.921904
	19	Heo,2014	1.006000	0.994000	1.017000	0.005982	0.006018	0.016857	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	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

Table S5 The p-value calculation process for each study using RR, CI low and CI high. (continued)

	Number	Study ID	RR	CI low	CI high	InRR	InCI low	lnCI high	SE	z	p-values
	1	Atkinson,2016	1.013000	0.993000	1.033000	0.012916	0.007025	0.032467	0.010074	1.282079	0.199815
	2	Geng,2013	1.002000	0.983000	1.021000	0.001998	0.017146	0.020783	0.009676	0.206497	0.836403
	3	Ostro,2015a	1.090000	1.004000	1.183000	0.086178	0.003992	0.168054	0.041852	2.059084	0.039486
	4	Ostro,2015a	1.064000	1.020000	1.110000	0.062035	0.019803	0.104360	0.021571	2.875902	0.004029
	5	Sarnat,2015	0.995000	0.969000	1.022000	0.005013	0.031491	0.021761	0.013585	0.368983	0.712140
	6	Huang,2012	1.005000	0.993000	1.017000	0.004988	0.007025	0.016857	0.006092	0.818666	0.412977
	7	Son,2012	0.989000	0.956000	1.024000	0.011061	0.044997	0.023717	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	0.090672	0.415806	0.677552
	15	Kim,2012	1.100000	0.949000	1.270000	0.095310	0.052346	0.239017	0.074327	1.282302	0.199737
	16	Cakmak,2009	1.036000	1.031000	1.041000	0.035367	0.030529	0.040182	0.002462	14.36291	3.2036*10-45
	17	Wang,2019a	1.038000	1.017000	1.059000	0.037296	0.016857	0.057325	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

Table S6 Results of risk of bias assessment.

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

Table S6 Results of risk of bias assessment. (continued)

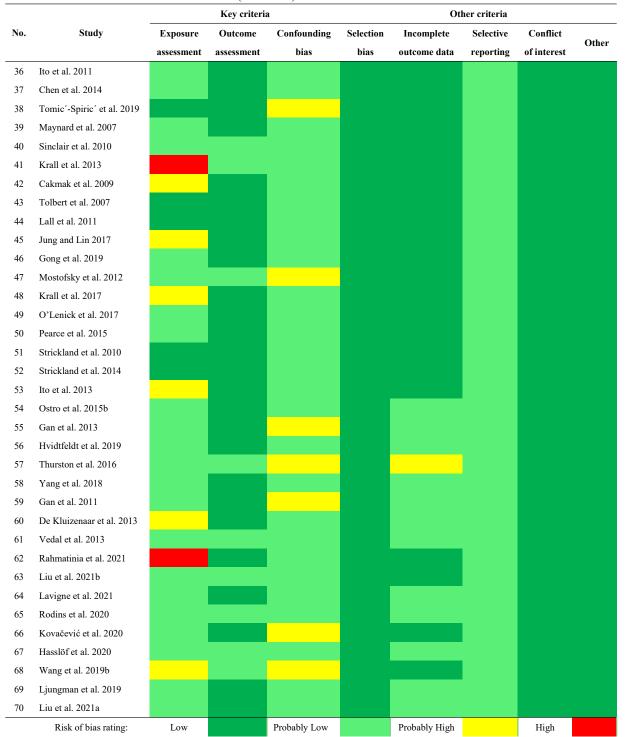


Table S7 Details of risk of bias assessment.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
1	Atkinson	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
	et al. 2016	All of the pollutants were	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			levels.	suggests study		
			Classification of				was free of		
			Diseases,10th				selective		
			revision-ICD10: I00-I99)				report.		
			and respiratory (ICD10:						
			J00-J99) diseases.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
2	Bell et al.	Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
	2014	BC measured from filters	The study used the	Models adjusted	Data obtained	Daily counts	There was	The authors	No other
		collected daily using	Medicare beneficiary	for time	from records of	for hospital	insufficient	declare no	potential
		optical reflectance.	denominator file from the	(seasonality,	individuals ≥65	admissions	information	conflict of	sources of
		Monitors from 5 sites	Centers for Medicare and	long-term trend),	years of age	were obtained,	about	interest.	bias
		across 4 counties were	Medicaid Services. Cause	day of week,	enrolled in the	so likely have	selective		identified.
		used. Sampling occurred	of admission was	temperature, and	Medicare	all outcome	outcome to		
		daily, with some missing	determined by principal	dew point.	fee-for-service	data. However,	judge for low		
		periods, for Hartford,	discharge diagnosis code		plan during	any potential	risk, but		
		New Haven, and	according to International		August 2000 to	errors or	indirect		
		Springfield, and every	Classification of		February 2004.	missing data	evidence that		
		third day for Bridgeport	Diseases, Ninth Revision,			did not depend	suggests study		
		and Danbury. Days with	Clinical Modification			on air pollution	was free of		
		missing data were	(ICD-9-CM; National			levels.	selective		
		omitted from analysis	Center for Health				report.		
		(the number of missing	Statistics 2006).						
		data was not reported).							

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
4	Geng et	Single, central-site	Health data were	Models included	Data consisted of	Daily counts	There was	The authors	No other
	al. 2013	monitor. Daily BC and	obtained from Shanghai	time (seasonality,	all causes	for death were	insufficient	declare no	potential
		PM _{2.5} were measured	Municipal Center of	long-term trend),	(excluding	obtained, so	information	conflict of	sources of
		continuously and 24hr	Disease Control and	temperature,	accidents or	likely have all	about	interest.	bias
		averaged was estimated	Prevention database. The	humidity and day	injuries) deaths	outcome data.	selective		identified.
		if >75% of the 1hr values	causes of death were	of week.	during over the	However, any	outcome to		
		was available for that	coded according to the		course of the	potential errors	judge for low		
		day. Missing data was not	International		study.	or missing data	risk, but		
		replaced by other values.	Classification of			did not depend	indirect		
			Diseases, Revision 10			on air pollution	evidence that		
			(ICD 10).			levels.	suggests study		
							was free of		
							selective		
							report.		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
5	Hua et al.	Daily 24h average PM _{2.5}	Daily asthma hospital	Adjusted for	Study included	Daily counts	There was	Authors	No other
	2014	and BC data was	admission data was	long-term and	all asthma	for asthma	insufficient	declared no	potential
		obtained from a fixed-site	obtained from Shanghai	seasonal trend, day	hospital	hospital	information	competing	sources of
		station. The study only	Children's Medical	of week,	admissions of	admissions of	about	financial	bias
		used the actual collected	Center. Dates of	temperature and	children ≤ 14	children were	selective	interests.	identified.
		data and did not fill in the	admission and discharge,	relative humidity.	years of age from	obtained, so	outcome to		
		missing data for PM _{2.5}	and diagnoses using the		Shanghai	likely have all	judge for low		
		and black carbon.	International		Children's	outcome data.	risk, but		
			Classification of		Medical Center	However, any	indirect		
			Diseases, Revision 10.		between1	potential errors	evidence that		
					January 2007 and	or missing data	suggests study		
					31 July 2012 in	did not depend	was free of		
					nine urban	on air pollution	selective		
					districts of	levels.	report.		
					Shanghai.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Low	Low	Low	Probably Low	Low	Low
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: I00199), 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.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
7	Samoli et	Daily concentrations of	Based on the primary	Adjusted for long	Study included	Daily counts	There was	Authors	No other
	al. 2016	BC and EC were	discharge diagnosis, daily	term and seasonal	all cardiovascular	for all	insufficient	declared no	potential
		collected from the	numbers of admissions	trends,	and respiratory	emergency	information	competing	sources of
		ClearfLo project,	for cardiovascular disease	temperature,	hospital	hospital	about	interests.	bias
		supplemented by local	(International	relative humidity,	admissions in	admissions	selective		identified.
		measurements made at	Classification of	regulated	London, UK	were obtained,	outcome to		
		the North Kensington	Diseases, 10th	pollutants (PM ₁₀ ,	between 2011	so likely have	judge for low		
		urban background site.	revision-ICD-10:	PM _{2.5} , NO ₂ , SO ₂	and 2012.	all outcome	risk, but		
		Number of days of	I00-I99) for those aged	and O ₃), day of the		data. However,	indirect		
		observation for BC: 629	15-64 (adult) and 65+	week and public		any potential	evidence that		
		(BC urban in PM _{2.5}) and	years (elderly), and	holidays.		errors or	suggests study		
		702 (BC in PM _{2.5})	respiratory diseases			missing data	was free of		
		between 2011 and 2012	(ICD-10: J00-J99) for			did not depend	selective		
		(<25% missing data).	those aged 0-14 years			on air pollution	report.		
			(paediatric), adult and the			levels.			
			elderly were calculated.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
8	Zanobetti	Ambient BC from one	The study extracted data	Adjusted for	Data consisted of	Daily counts	There was	Authors	No other
	and	monitor. The hourly	on all hospital admissions	temperature, day	all U.S. Medicare	for hospital	insufficient	declared no	potential
	Schwartz	measurements for BC and	for residents of the	of the week,	hospital	admissions	information	competing	sources of
	2006	PM _{2.5} were not complete.	Boston Metropolitan area	seasonality,	admissions in the	were obtained,	about	interests.	bias
		Missing values were	who were admitted to the	long-term trends,	Boston	so likely have	selective		identified.
		replaced with the	hospital (in the Boston	humidity,	Metropolitan	all outcome	outcome to		
		predicted values.	area) with a primary	barometric	area for	data. However,	judge for low		
		Additionally BC data was	diagnosis of MI	pressure, and the	myocardial	any potential	risk, but		
		missing from March 1997	(International	extinction	infarction during	errors or	indirect		
		to March 1999 and was	Classification of	coefficient.	the study	missing data	evidence that		
		not included in the study.	Diseases, 9th		duration.	did not depend	suggests study		
			revision-ICD-9:410), and			on air pollution	was free of		
			pneumonia (ICD-9:			levels.	selective		
			480–487), from Medicare				report.		
			billing records for the				_		
			years 1995–1999.						
			, ,						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
9	Liu et al.	EC were collected from a	Emergency department	Adjusted for time	Study included	Daily counts	There was	Authors	No other
	2016a	single monitor on a	visit data was obtained	(long-term and	daily counts of	for emergency	insufficient	declared no	potential
		one-in-three or one-in-six	from the Blue Cross Blue	seasonal trend),	emergency	department	information	potential	sources of
		day schedule. EC were	Shield Texa. International	day of week,	department visits	visits were	about	competing	bias
		measured for 566 days	Classification of Diseases	temperature, dew	for Greater	obtained, so	selective	financial	identified.
		from April 02, 2009, to	9th Revision (ICD-9)	point and	Houston from	likely have all	outcome to	interests.	
		December 30, 2013,	diagnosis codes were	population growth.	claims data	outcome data.	judge for low		
		<25% missing for the	used to classify outcome		insured from	However, any	risk, but		
		frequency of sampling.	groups.		January 1, 2008	potential errors	indirect		
					through	or missing data	evidence that		
					December 31,	did not depend	suggests study		
					2013.	on air pollution	was free of		
						levels.	selective		
							report.		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
10	Liu et al.	EC were collected from a	Hospital admission data	Adjusted for time,	Study included	Daily counts	There was	Authors	No other
	2016b	single monitor on a	was obtained from the	day of week,	all hospital	for HA were	insufficient	declared no	potential
		one-in-three or one-in-six	Blue Cross Blue Shield	temperature,	admissions	obtained, so	information	competing	sources of
		day schedule. EC were	Texa. International	seasonaility,	obtained from	likely have all	about	financial	bias
		measured for 566 days	Classification of Diseases	humidity and	billing claims of	outcome data.	selective	interests.	identified.
		from April 02, 2009, to	9th Revision (ICD-9)	population growth.	Blue Cross Blue	However, any	outcome to		
		December 30, 2013,	diagnosis codes were		Shield Texa	potential errors	judge for low		
		<25% missing for the	used to classify outcome		enrollees for	or missing data	risk, but		
		frequency of sampling.	groups.		Greater Houston	did not depend	indirect		
					from January 1,	on air pollution	evidence that		
					2008 to	levels.	suggests study		
					December 31,		was free of		
					2013.		selective		
							report.		

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
11	Sarnat et al. 2015			0			1		

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	Low	Probably Low	Low	Low
12	Kim et al.	PM _{2.5} mass and chemical	All individual hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
	2012	constituents were	admission records during	days from the start	all cardiovascular	for hospital	insufficient	declare they	potential
		measured daily at one	the study period were	of the study, day of	hospital	admission were	information	have no	sources of
		residential monitoring	extracted from	week, seasonality,	admissions over	obtained, so	about	actual or	bias
		station located on the	nonelective hospital	long-term trends,	the course of the	likely have all	selective	potential	identified.
		roof of an elementary	admission discharge data	daily average	study.	outcome data.	outcome to	competing	
		school building in	obtained from the	temperature and		However, any	judge for low	financial	
		Denver. The observations	Colorado Hospital	relative humidity.		potential errors	risk, but	interests.	
		of EC was 1809 days	Association. The			or missing data	indirect		
		during 2003-2007	International			did not depend	evidence that		
		(missing data <25%).	Classification of			on air pollution	suggests study		
			Diseases, Ninth			levels.	was free of		
			Revision(ICD-9) codes				selective		
			were used to define				report.		
			cardiovascular hospital						
			admissions (codes						
			390–459) and respiratory						
			hospital admissions						
			(codes 460–519).						

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

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	Low	Probably Low	Low	Low
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
	2015	PM _{2.5} samples were	metropolitan Denver	for longer-term	all deaths over	for death were	insufficient	authors has	potential
		collected from single,	were computed from the	temporal trend, as	the course of the	obtained, so	information	any actual	sources of
		central-site monitor. The	Colorado Health	time since the	study in a	likely have all	about	or potential	bias
		observations of EC was	Information Dataset	study began, day	defined	outcome data.	selective	competing	identified.
		1809 days from 2003	compiled by the Colorado	of week, and daily	geographical	However, any	outcome to	interests.	
		through 2007 (missing	Department of Public	temperature and	area.	potential errors	judge for low		
		data <25%).	Health and Environment.	humidity.		or missing data	risk, but		
			Data included cause of			did not depend	indirect		
			death by the International			on air pollution	evidence that		
			Classification of Diseases			levels.	suggests study		
			10th Revision (ICD-10)				was free of		
			code.				selective		
							report.		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
16	Peng et al.	Ambient EC obtained	Daily counts of hospital	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
	2009	from Speciation Trends	admissions were obtained	weather (i.e.,	all cardiovascular	for hospital	insufficient	declare they	potential
		Network monitors and	from billing claims of	temperature, dew	hospital	admission were	information	have no	sources of
		either from central site or	enrollees in the U.S.	point temperature),	admissions	obtained, so	about	competing	bias
		averaged over a county.	Medicare system. Each	day of week,	during over the	likely have all	selective	financial	identified.
		Air pollution	billing claim contains the	unobserved	course of the	outcome data.	outcome to	interests.	
		concentrations were	date of service, disease	seasonal factors,	study.	However, any	judge for low		
		measured on a 1-in-3-day	classification using	and long-term		potential errors	risk, but		
		schedule in the national	International	trends.		or missing data	indirect		
		air monitoring stations	Classification of			did not depend	evidence that		
		and on a 1-in-6-day	Diseases, 9th Revision			on air pollution	suggests study		
		schedule in the state and	(ICD-9) codes (Centers			levels.	was free of		
		local air monitoring	for Disease Control and				selective		
		stations. Study removed	Prevention 2008).				report.		
		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.							

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
17	Levy et al.	The U.S. Environmental	Hospital admissions data	Adjusted for time	Study included	Daily counts of	There was	No	No other
	2012	Protection Agency	were obtained from	(seasonality,	people who died	hospital	insufficient	competing	potential
		established the PM	billing claims information	long-term trends),	any day between	admissions	information	financial	sources of
		Speciation Trends	for US Medicare	seasonality, day of	2000 and 2008 in	were obtained	about	interests.	bias
		Network (STN) to	enrollees in 119 counties	the week and	119 US counties.	from billing	selective		identified.
		measure more than 50	for the years 2000–2008.	dew-point		claims	outcome to		
		PM _{2.5} chemical	The Medicare billing	temperature.		information, so	judge for low		
		components, in addition	claims data were			likely have all	risk, but		
		to total mass. The STN	classified into disease			outcome data.	indirect		
		includes > 50 national air	categories according to			However, any	evidence that		
		monitoring stations	their International			potential errors	suggests study		
		(NAMS) and > 200 state	Classification of			or missing data	was free of		
		and local air monitoring	Diseases, Ninth Revision			did not depend	selective		
		stations (SLAMS). Air	(ICD-9), codes.			on air pollution	report.		
		pollution concentrations				levels.			
		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.						_	

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	Low	Probably Low	Low	Low
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
	2012	obtained from a single,	obtained from the	for time (long-term	all cardiovascular	for death were	insufficient	declare they	potential
		central-site monitor. The	National Statistical	trends and	deaths over the	obtained, so	information	have no	sources of
		monitoring system	Office. The study	seasonality), day	course of the	likely have all	about	actual or	bias
		produces hourly	classified mortality data	of week,	study.	outcome data.	selective	potential	identified.
		estimates of PM _{2.5} total	into all causes of death	temperature and		However, any	outcome to	competing	
		mass, and PM _{2.5} levels of	[International	relative humidity.		potential errors	judge for low	financial	
		EC. Daily data was	Classification of			or missing data	risk, but	interests.	
		available and no missing	Diseases, 10th Revision			did not depend	indirect		
		data was reported.	(ICD-10; codes			on air pollution	evidence that		
			A00–R99),			levels.	suggests study		
			cardiovascular causes				was free of		
			(codes I00-I99), and				selective		
			respiratory causes (codes				report.		
			J00–J99)] (World Health						
			Organization 2007).						

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

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

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Low	Low	Low	Probably Low	Low	Low
22	Lin et al.	The concentrations of	Daily mortality data from	Adjusted for	Study included	Daily counts	There was	The authors	No other
	2016a	different particle size	1 January 2007 to 31	public holidays,	daily	for death were	insufficient	declare they	potential
		fractions and PM _{2.5}	December 2011 were	day of the week,	cardiovascular	obtained, so	information	have no	sources of
		chemical constituents	obtained from	influenza	mortality data	likely have all	about	actual or	bias
		were measured at two air	Guangdong Provincial	outbreaks,	from 1 January	outcome data.	selective	potential	identified.
		monitoring stations. EC	Center for Disease	seasonal patterns	2007 to 31	However, any	outcome to	competing	
		were measured for four	Control and Prevention.	and long-term	December 2011	potential errors	judge for low	financial	
		months of each year from	The cause of death was	trends, temperature	in Guangzhou.	or missing data	risk, but	interests.	
		2007 through 2010.	coded using the	and relative		did not depend	indirect		
		During the period	International	humidity.		on air pollution	evidence that		
		2009-2011, the	Classification of			levels.	suggests study		
		proportion of missing	Diseases, Tenth Revision				was free of		
		data was very low	(ICD-10). Mortality from				selective		
		(ranging from 1% to 2%).	cardiovascular diseases				report.		
		There were about 20 days	(ICD-10:I00-I99) were						
		without chemical	extracted to construct the						
		constituents records and	time series.						
		were treated as missing							
		observations.							

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	Low	Probably Low	Low	Low
23	Cao et al.	Daily concentrations of	The study obtained	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
	2012	EC was obtained from a	numbers of deaths in	long-term and	all nonaccidental	for death were	insufficient	declare they	potential
		single monitoring site.	Xi'an for each day from	seasonal trends,	causes deaths	obtained, so	information	have no	sources of
		The observations of EC	the Shanxi Provincial	day of week,	during over the	likely have all	about	actual or	bias
		was 1749 in 1827 days	Center for Disease	temperature,	course of the	outcome data.	selective	potential	identified.
		(missing data <25%).	Control and Prevention	humidity, and SO ₂	study.	However, any	outcome to	competing	
			(SPCDCP). SPCDCP	and NO ₂		potential errors	judge for low	financial	
			staff then classify the	concentrations.		or missing data	risk, but	interests.	
			cause of death according			did not depend	indirect		
			to the International			on air pollution	evidence that		
			Classification of			levels.	suggests study		
			Diseases, 10th Revision				was free of		
			[ICD-10; World Health				selective		
			Organization (WHO)				report.		
			1992] as due to total						
			nonaccidental causes						
			(ICD-10 codes						
			A00–R99),						
			cardiovascular diseases						
			(I00–I99), respiratory						
			diseases(J00–J98), or						
			injury (S00–T98).						

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	Low	Probably Low	Low	Low
24	Klemm et	Daily 24-hr average EC	Records of individual	Adjusted for time	Study included	Daily counts	There was	Authors	No other
	al. 2011	measurements are	deaths were provided by	(seasonality,	all nonaccidental	for death were	insufficient	declared no	potential
		available for Atlanta	the Georgia Department	long-term trends),	deaths during	obtained, so	information	competing	sources of
		during the study period.	of Human Resources.	temperature, and	over the course	likely have all	about	financial	bias
		The observations of EC	Cause of death is	day of the week.	of the study.	outcome data.	selective	interests.	identified.
		was 3317 days from	categorized using the			However, any	outcome to		
		August 1998 to	International			potential errors	judge for low		
		December 31, 2007.	Classification of			or missing data	risk, but		
		Missing data <25%.	Diseases, 10th edition			did not depend	indirect		
		There was no information	(ICD-10), including			on air pollution	evidence that		
		for monitor stations.	circulatory conditions			levels.	suggests study		
			(I00–I99), respiratory				was free of		
			conditions (J00–J99),				selective		
			malignant neoplasm				report.		
			(cancer; C00–D48), or						
			other nonaccidental						
			causes (A00-R99,						
			excluding cardiovascular,						
			respiratory, or cancer						
			causes).						

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	Low	Probably Low	Low	Low
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
	2011	obtained from a single,	International	for time,	all cardiovascular	for death were	insufficient	declare they	potential
		central-site monitor.	Classification of	seasonality and	deaths over the	obtained, so	information	have no	sources of
		Daily data was available	Diseases, version 10	long-term trends,	course of the	likely have all	about	actual or	bias
		and no missing data was	(ICD10; World Health	day of week,	study.	outcome data.	selective	potential	identified.
		reported.	Organization 2007), daily	temperature, and		However, any	outcome to	competing	
			death counts were	humidity.		potential errors	judge for low	financial	
			aggregated to			or missing data	risk, but	interests.	
			nonaccidental allcause			did not depend	indirect		
			deaths (ICD10, codes			on air pollution	evidence that		
			A00 through R99),			levels.	suggests study		
			cardiovascular deaths				was free of		
			(ICD10, codes I01				selective		
			through I99), and				report.		
			respiratory deaths						
			(ICD10, codes J00						
			through J99).						

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	Low	Probably Low	Low	Low
26	Winquist	Daily EC and BC were	Individual-level data	Adjusted for time	Study included	Daily counts	There was	Authors	No other
	et al. 2015	from a single monitor	were obtained from the	trends, day of	emergency	for emergency	insufficient	declared no	potential
		site. All species of	Missouri Hospital	week, holidays,	department visits	department	information	competing	sources of
		pollutant statistics are	Association for all	season,	in St Louis	visit were	about	financial	bias
		missing less than 5%.	emergency department	temperature and	metropolitan	obtained, so	selective	interests.	identified.
			visits to 36 of 43	dew point.	statistical area	likely have all	outcome to		
			acute-care non-federal		during 1 June	outcome data.	judge for low		
			hospitals with emergency		2001 through 30	However, any	risk, but		
			department visits in the		April 2003.	potential errors	indirect		
			16-county St Louis			or missing data	evidence that		
			metropolitan statistical			did not depend	suggests study		
			area during 1 June 2001			on air pollution	was free of		
			through 30 April 2003.			levels.	selective		
			Cardiorespiratory				report.		
			outcomes of interest were						
			defined based on the						
			primary ICD-9						
			(International						
			Classification of						
			Diseases, version 9)						
			diagnosis code for the						
			visit.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
27	Ostro et	Each of the six counties	Daily mortality data were	Adjusted for time	Data consisted of	Daily counts	There was	The authors	No other
	al. 2007	had two monitors	obtained from the	trend, day of week,	all cardiovascular	for death were	insufficient	declare they	potential
		measuring PM _{2.5}	California Department of	seasonality,	deaths over the	obtained, so	information	have no	sources of
		components and mass.	Health Services, Center	long-term trends,	course of the	likely have all	about	competing	bias
		Fresno, Kern, Riverside,	for Health Statistics. The	temperature and	study.	outcome data.	selective	financial	identified.
		and Sacramento Counties	study determined daily	humidity.		However, any	outcome to	interests.	
		reported data every third	total mortality counts for			potential errors	judge for low		
		day, whereas San Diego	those > 65 years of age			or missing data	risk, but		
		and Santa Clara Counties	and for deaths from			did not depend	indirect		
		reported data every sixth	respiratory disease			on air pollution	evidence that		
		day. For the speciation	[International			levels.	suggests study		
		analyses, the number of	Classification of				was free of		
		observation days	Diseases, 10th Revision				selective		
		available ranged from	(ICD10; World Health				report.		
		243 (San Diego County)	Organization 1993) codes						
		to 395 (Sacramento	J00–J98] and						
		County) from 2000 to	cardiovascular disease						
		2003. There was no	(codes I00–I99).						
		specific information							
		about missing data.							

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	Low	Probably Low	Low	Low
28	Tolbert et	Daily 24h EC from a	Computerized billing	Adjusted for time	Study included	Daily count for	There was	Authors	No other
	al. 2000	single monitor site. The	record data are being	(seasonality,	emergency	emergency	insufficient	declared no	potential
		observation of EC was	obtained from the	long-term trends),	department visits	department	information	competing	sources of
		356 in 365 days, missing	emergency department	temperature, dew	of the	visits were	about	financial	bias
		data <25%.	visits participating in the	point, and day of	participating	obtained, so	selective	interests.	identified.
			study. Several case	week.	hospitals in the	likely have all	outcome to		
			groups are being defined		Atlanta	outcome data.	judge for low		
			using the primary ICD-9		Metropolitan	However, any	risk, but		
			(International		Statistical Area,	potential errors	indirect		
			Classification of		including 33	or missing data	evidence that		
			Diseases, 9th Revision)		hospitals	did not depend	suggests study		
			diagnostic code.		between January	on air pollution	was free of		
					1 1993-August	levels.	selective		
					31 2000, 4		report.		
					hospitals				
					between January				
					1 1993-February				
					30 2000.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
29	Wang and	The hourly data were	This study obtained	Adjusted for	Study included	Daily counts	There was	Authors	No other
	Lin 2016	simply averaged to	universal health insurance	temperature,	elderly (≧65	for elderly	insufficient	declared no	potential
		calculate the daily	claims from the National	relative humidity,	elderly (≥03	mortality and	information	competing	sources of
		average data for PM ₁₀ ,	Health Research Institute	wind speed,	years) mortality	all population	about	financial	bias
		PM _{2.5} monitored at 13	(NHRI) and vital	barometric	from 2004 to	emergency	selective	interests.	identified.
		general air quality	statistics from the	pressure, holidays,	2008 and all	room visits	outcome to		
		monitoring stations	Ministry of Health and	day of the week,	population EVR	were obtained,	judge for low		
		located in a densely	Welfare from 2004 to	pneumonia and	from 2004 to	so likely have	risk, but		
		populated area in Taipei.	2008. Death causes were	influenza.	2010 in Taipei,	all outcome	indirect		
		Hourly concentrations of	coded according to the		Taiwan.	data. However,	evidence that		
		EC were detected by	diagnoses of the 9th			any potential	suggests study		
		series 5400 Monitor. Very	revision of International			errors or	was free of		
		few missing values in the	Classification of Diseases			missing data	selective		
		database were omitted as	(ICD-9). Disease			did not depend	report.		
		the daily average was	diagnoses were based on			on air pollution			
		calculated.	the International			levels.			
			Classification of Diseases						
			with Clinical						
			Modification, Ninth						
			Revision (ICD-9 CM).						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete 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	selective	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	indirect		
			Diseases, 9th Revision		2004 (not all	participating.	evidence that		
			(ICD-9), diagnosis codes:		hospitals	However, any	suggests study		
			acute bronchitis or		contributed the	potential errors	was free of		
			bronchiolitis (code 466);		full period), and	or missing data	selective		
			pneumonia (codes		from the Georgia	did not depend	report.		
			480–486); and upper		Hospital	on air pollution			
			respiratory infection		Association for	levels.			
			(codes 460–465).		the period				
					January 1, 2005,				
					to June 30, 2010.				

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

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	Low	Probably Low	Low	Low
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	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	There was insufficient information about selective outcome to judge for low risk, but indirect	No competing financial interests.	No other potential sources of bias identified.
			cause of death as identified by the International Classification of Diseases, Ninth Revision (ICD-9, World Health Organization, Geneva).			on air pollution levels.	evidence that suggests study was free of selective report.		

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
34	Lin et al.	EC was from a single	Daily mortality data were	Adjusted for	Study included	Daily counts	There was	Authors	No other
	2016b	monitor site for four	obtained from the death	long-term trends,	the residents who	for death were	insufficient	declared no	potential
		months of each year from	registry system. The	seasonality,	died of ischemic	obtained, so	information	conflict of	sources of
		2007 to 2010. Missing	cause of death was coded	temperature,	or hemorrhagic	likely have all	about	interest.	bias
		data for the particle	using the International	humidity, day of	strokes in urban	outcome data.	selective		identified.
		concentration was very	Classification of	week and public	districts of	However, any	outcome to		
		low (ranging from 1% to	Diseases, Tenth Revision	holidays.	Guangzhou	potential errors	judge for low		
		2%).	(ICD-10). Mortality from		between 2007	or missing data	risk, but		
			stroke (ICD-10:I60–I66),		and 2011.	did not depend	indirect		
			and sub-categories,			on air pollution	evidence that		
			including ischemic stroke			levels.	suggests study		
			(ICD-10:I63–I66), and				was free of		
			hemorrhagic stroke				selective		
			(ICD-10: I60–I62) were				report.		
			extracted to construct the						
			time series.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
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
	2016b	had two monitors	California residents were	temperature,	daily	for death were	insufficient	declared no	potential
		measuring components of	obtained from the	humidity and day	cardiovascular	obtained, so	information	competing	sources of
		PM _{2.5} . Fresno, Kern,	California Department of	of the week.	mortality for all	likely have all	about	interests.	bias
		Riverside and	Health Services, Center		California	outcome data.	selective		identified.
		Sacramento counties	for Health Statistics.		residents from 1	However, any	outcome to		
		reported 24-hour average	Daily counts of deaths		January 2000 to	potential errors	judge for low		
		EC in PM _{2.5} every third	from cardiovascular		31 December	or missing data	risk, but		
		day; San Diego and Santa	disease (International		2003.	did not depend	indirect		
		Clara counties reported	Classification of			on air pollution	evidence that		
		data every sixth day. The	Diseases, Tenth Revision			levels.	suggests study		
		study included only	(ICD10) =I00–I99) were				was free of		
		species for which at least	calculated.				selective		
		50% of the observations					report.		
		were above the level of							
		detection.							

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	Low	Probably Low	Low	Low
36	Ito et al.	Ambient EC obtained	Hospitalizations and	Model adjusted for	Data consisted of	Daily counts	There was	The authors	No other
	2011	from multiple monitors	mortality data were	temporal trends	all cardiovascular	for death and	insufficient	declare they	potential
		and the average of data	available at the New York	and seasonal	hospital	hospitalization	information	have no	sources of
		from multiple monitors	City Department of	cycles, immediate	admissions over	were obtained,	about	actual or	bias
		was computed using the	Health and Mental	and delayed	the course of the	so likely have	selective	potential	identified.
		24hr average values. The	Hygiene. The relevant	temperature	study.	all outcome	outcome to	competing	
		sampling frequency of	variables available in the	effects, and day of		data. However,	judge for low	financial	
		the chemical speciation	electronic discharge	the week.		any potential	risk, but	interests.	
		data was every third day.	abstract for each patient			errors or	indirect		
		Daily data was available	included date of			missing data	evidence that		
		and no missing data was	admission and			did not depend	suggests study		
		reported.	International			on air pollution	was free of		
			Classification of			levels.	selective		
			Diseases, Nine Revision				report.		
			(ICD9) discharge						
			diagnosis code. The						
			International						
			Classification of						
			Diseases, Tenth Revision						
			(ICD10) codes for						
			determining cause of						
			death.						

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	Low	Probably Low	Low	Low
37	Chen et al. 2014	Hourly mass concentrations of PM _{2.5} and the four PM _{2.5} constituents obtained from a Supersite (single,	The counts of daily emergency room visits were obtained from the National Taiwan University Hospital. The	Models adjusted for time, day of week, temperature, seasonality and relative humidity.	Data consisted of all emergency department visits during the study period for	Daily counts for emergency room visit were obtained, so likely have	There was insufficient information about selective	No competing financial interests.	No other potential sources of bias identified.
		central site monitoring location). The observations of EC was 1599 in 1705 days (missing data <25%).	emergency room visit data were coded regarding the discharge diagnosis using the International Classification of Disease, 9th revision (ICD-9).		ischemic and hemorrhagic stroke.	all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Low	Low	Probably High	Low	Low	Probably Low	Low	Low
38	Tomic'-Sp	Average daily	Emergency department	Adjusted for	Study included	All counts for	There was	Authors	No other
	iric' et al.	concentrations of BC in	visits data were obtained	temperature,	emergency	emergency	insufficient	declared no	potential
	2019	micrograms per cubic	from the Health Center	humidity, and air	department visit	department	information	competing	sources of
		meter were measured by	Užice, either from the	pressure.	for allergic	visits were	about	financial	bias
		three automatic ambient	emergency department		rhinitis and	obtained, so	selective	interests.	identified.
		air quality monitoring	visits in Užice, Sevojno,		allergic asthma	likely have all	outcome to		
		stations. There was no	and Kosjeri' c, or from a		from 1 July 2012	outcome data.	judge for low		
		information about	general hospital in Užice.		to 30 June 2014	However, any	risk, but		
		missing data.	The inclusion criteria		in the Zlatibor	potential errors	indirect		
			were adults aged 18 years		District, Western	or missing data	evidence that		
			and older with the		Serbia.	did not depend	suggests study		
			diagnosis of allergic			on air pollution	was free of		
			rhinitis (International			levels.	selective		
			Classification of				report.		
			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.						

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
40	Sinclair et	Daily 24-hr averages EC	Daily outpatient visits	Adjusted for	Study included	Daily counts	There was	No	No other
	al. 2010	was from a single	were obtained from the	season, day of	daily outpatient	for outpatient	insufficient	competing	potential
		monitor site. The total	electronic patient data	week, federal	visits for acute	visits were	information	financial	sources of
		observed rate of EC was	warehouse of a	holidays, study	respiratory	obtained, so	about	interests.	bias
		95.2%.	not-for-profit,	month, time,	diseases from the	likely have all	selective		identified.
			group-model managed	temperature and	electronic patient	outcome data.	outcome to		
			care organization (MCO)	dew point.	data warehouse	However, any	judge for low		
			in the metropolitan		of a	potential errors	risk, but		
			Atlanta area between		not-for-profit,	or missing data	indirect		
			August 1, 1998 and		group-model	did not depend	evidence that		
			December 31, 2002.		managed care	on air pollution	suggests study		
			Visits that met acute visit		organization	levels.	was free of		
			definition and that had a		(MCO) in the		selective		
			visit diagnosis code of		metropolitan		report.		
			asthma, upper respiratory		Atlanta area				
			infection (URI), or lower		between August				
			respiratory infection		1, 1998 and				
			(LRI) were included in		December 31,				
			the study.		2002.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		High	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
41	Krall et al.	Monitors typically	All-cause mortality data	Adjusted for	Study included	Daily counts	There was	The authors	No other
	2013	measure PM _{2.5}	(excluding accidental	temperature, day	all death	for death were	insufficient	declare they	potential
		constituent	deaths) were aggregated	of week, long-term	(excluding	obtained, so	information	have no	sources of
		concentrations every	from death certificate	and seasonal	accidental	likely have all	about	actual or	bias
		third or sixth day. Some	data obtained from the	trends.	deaths) for 108	outcome data.	selective	potential	identified.
		communities with a	National Center for		urban	However, any	outcome to	competing	
		single monitor. The	Health Statistics for 2000		communities	potential errors	judge for low	financial	
		observation of EC was	to 2005.		from 2000 to	or missing data	risk, but	interests.	
		58-921 days,some			2005.	did not depend	indirect		
		communities had >25%				on air pollution	evidence that		
		missing data.				levels.	suggests study		
							was free of		
							selective		
							report.		

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

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

Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
	Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
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
2011	obtained from two	admissions data was	season, wintertime	all cardiovascular	for hospital	insufficient	declare they	potential
	monitors. Daily data was	based on codes from the	influenza episode,	hospital	admission were	information	have no	sources of
	available and no missing	International	weather, day of	admissions over	obtained, so	about	actual or	bias
	data was reported.	Classification of	week, and other	the course of the	likely have all	selective	potential	identified.
		Diseases, revision 9	possible	study.	outcome data.	outcome to	competing	
		(ICD-9).	confounders (e.g.,		However, any	judge for low	financial	
			federal holidays).		potential errors	risk, but	interests.	
					or missing data	indirect		
					did not depend	evidence that		
					on air pollution	suggests study		
					levels.	was free of		
						selective		
						report.		
	Lall et al.	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Low The categorization of the admissions data was based on codes from the International Classification of Diseases, revision 9	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Low Low Probably Low Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible (ICD-9). Lall et al. Daily EC data were obtained from two season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g.,	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Low Low Daily EC data were obtained from two admissions data was available and no missing data was reported. Low Dow Model adjusted for season, wintertime influenza episode, weather, day of data was reported. Classification of week, and other the course of the Diseases, revision 9 possible study. (ICD-9). Confounders (e.g.,	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Classification of Diseases, revision 9 (ICD-9). Confounding bias outcome data Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Confounding bias outcome data Confounding bias outcome data Low Low Model adjusted for season, wintertime influenza episode, weather, day of week, and other possible confounders (e.g., federal holidays). Classification of possible confounders (e.g., federal holidays).	Lall et al. 2011 Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Classification of Diseases, revision 9 (ICD-9). (ICD-9). Exposure assessment Confounding bias Selection bias Outcome data reporting	Lall et al. Daily EC data were obtained from two monitors. Daily data was available and no missing data was reported. Classification of Diseases, revision 9 (ICD-9). The categorization of the admissions of the possible confounders (e.g., federal holidays). Exposure assessment Low Low Low Low Low Data consisted of paily counts of hospital admission were admission were information all cardiovascular for hospital admission were obtained, so about actual or selective potential outcome data. Classification of Diseases, revision 9 (ICD-9). (ICD-9). Confounding bias Selection bias Outcome data Probably Low Low Probably Low Data consisted of all cardiovascular for hospital admission were obtained, so about actual or selective potential outcome data. However, any potential errors or missing data did not depend on air pollution levels. Federal holidays). Selection bias Outcome data Probably Low Low The categorization of the admissions declare they insufficient insufficient admission were obtained, so about actual or selective potential outcome data. However, any potential errors or missing data did not depend on air pollution levels. Federal holidays).

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

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	Low	Probably Low	Low	Low
46	Gong et	The 24-h mean BC	The disease data used in	Adjusted for	Study included	Daily counts	There was	Authors	No other
	al. 2019	concentrations data were	this study were collected	calendar effects,	all cardiovascular	for all deaths	insufficient	declared no	potential
		obtained from a single	from the Chinese Center	long-term trends,	mortality in	were obtained,	information	conflict of	sources of
		monitor site. During the	for Disease Control and	temperature,	Beijing obtained	so likely have	about	interest.	bias
		study period (2091 days),	Prevention, and included	humidity, day of	from the Chinese	all outcome	selective		identified.
		missing rate of BC was	all deaths in Beijing from	week, NO2 and	Center for	data. However,	outcome to		
		0.68%.	January 1, 2006 to	SO ₂ .	Disease Control	any potential	judge for low		
			December 31, 2011.		and Prevention	errors or	risk, but		
			Causes of death were		during January 1,	missing data	indirect		
			classified according to		2006 to	did not depend	evidence that		
			the International		December 31,	on air pollution	suggests study		
			Classification of		2011.	levels.	was free of		
			Diseases, 10th Edition				selective		
			(ICD-10) and data on				report.		
			cardiovascular diseases						
			(ICD-10 code: I00–I99)						
			were obtained.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably High	Low	Low	Probably Low	Low	Low
47	Mostofsky	Ambient EC obtained	Patients potentially	Model adjusted for	Population	Daily counts	There was	No	No other
	et al. 2012	from one monitor. BC	eligible for this study	seasonality,	consisted of	for emergency	insufficient	competing	potential
		concentrations were	were identified by	time-trends,	patients ≥21	department	information	financial	sources of
		measured continuously.	reviewing daily	temperature, dew	years of age	admission were	about	interests.	bias
		Daily data was available	emergency department	point temperature,	admitted to the	obtained, so	selective		identified.
		and no missing data was	admission logs, stroke	barometric	hospital with	likely have all	outcome to		
		reported.	service admission logs,	pressure and	neurologist-confi	outcome data.	judge for low		
			stroke service consult	chronic and	rmed ischemic	However, any	risk, but		
			logs, and hospital	slowly-varying	stroke and	potential errors	indirect		
			electronic discharge	potential	residing in the	or missing data	evidence that		
			records.	confounders.	Boston	did not depend	suggests study		
					metropolitan	on air pollution	was free of		
					region. Also	levels.	selective		
					patients had to		report.		
					reside within 40				
					km of the air				
					pollution				
					monitor.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	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	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		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	selective		
			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				
			(491,492,496), upper		metropolitan				
			respiratory infection		area, and the				
			(URI) (460–465, 466.0,		12-county Dallas				
			477), and asthma and/or		metropolitan				
			wheeze (493, 786.07).		area.				

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	Low	Probably Low	Low	Low
49	O'Lenick	The 24-hour average	Patient-level emergency	Adjusted for	Study included	Daily counts	There was	Competing	No other
	et al. 2017	concentration of EC was	department visit data	season, periods of	all emergency	for emergency	insufficient	interests:	potential
		evaluated. Pollutant	from 1 January 2002 to	hospital	department visit	department	information	None	sources of
		concentration estimates	31 December 2008 were	participation and	data acquired	visit were	about	declared.	bias
		were obtained by fusing	acquired from hospitals	holidays,	directly from	obtained, so	selective		identified.
		observational data from	located within the	temperature and	hospitals	likely have all	outcome to		
		available network	20-county metropolitan	mean dew point,	(2002–2004	outcome data.	judge for low		
		monitors with pollutant	area of Atlanta; Relevant	interaction terms	period) and the	However, any	risk, but		
		concentration simulations	data elements included	between season	Georgia Hospital	potential errors	indirect		
		from the Community	admission date,	and maximum	Association	or missing data	evidence that		
		Multi-Scale Air Quality	International	temperature and	(2005–2008	did not depend	suggests study		
		emissions-based chemical	Classification of Diseases	day of year.	period) located	on air pollution	was free of		
		transport model at	Ninth Revision (ICD-9)		within the	levels.	selective		
		12×12km grids over	diagnosis codes, age and		20-county		report.		
		Atlanta. 24-hour average	ZIP code of patient		metropolitan area				
		EC were evaluated. Daily	residence.		of Atlanta.				
		data was available and no							
		missing data was							
		reported.							

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	Low	Probably Low	Low	Low
50	Pearce et	Daily EC data were	The study obtained	Adjusted for year,	Study included	Daily counts	There was	The authors	No other
	al. 2015	obtained from a central	aggregate daily counts for	season, month, day	all emergency	for pediatric	insufficient	declare that	potential
		monitoring location in	pediatric asthma related	of the week,	department visits	asthma related	information	they have	sources of
		Atlanta. Daily data was	emergency department	hospital, holidays,	for pediatric	emergency	about	no	bias
		available and no missing	visits for children ages 5	temperature and	asthma of	department	selective	competing	identified.
		data was reported.	to 18 years from 41	dew point.	children ages 5 to	visits were	outcome to	interests.	
			hospitals within		18 years from 41	obtained, so	judge for low		
			metropolitan Atlanta; and		hospitals within	likely have all	risk, but		
			defined emergency		metropolitan	outcome data.	indirect		
			department visits for		Atlanta for study	However, any	evidence that		
			pediatric asthma as all		period.	potential errors	suggests study		
			visits with a code for			or missing data	was free of		
			asthma (493.0–493.9) or			did not depend	selective		
			wheeze (786.07) using			on air pollution	report.		
			the International			levels.			
			Classification of						
			Diseases, 9th Revision.						

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

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
53	Ito et al.	The study chose 150 U.S.	Using International	Adjusted for	Study included	Daily counts	There was	No conflict	No other
	2013	metropolitan statistical	Classification of	modeling of	all nonaccidental	for death and	insufficient	of interests.	potential
		areas where the data from	Diseases, 10th Revision	confounding	all-cause,	emergency	information		sources of
		at least one Chemical	(ICD-10) codes, the study	temporal trends	cardiovascular	hospitalization	about		bias
		Species Network monitor	aggregated daily death	(annual cycles and	disease and	were obtained,	selective		identified.
		were available. The	counts for the	influenza	respiratory	so likely have	outcome to		
		Chemical Species	nonaccidental all-cause,	epidemics),	deaths and	all outcome	judge for low		
		Network data for PM _{2.5}	cardiovascular disease	day-of-week	emergency	data. However,	risk, but		
		components were	and respiratory deaths.	patterns and	hospitalizations	any potential	indirect		
		available either every	Using International	temperature.	for the elderly	errors or	evidence that		
		third day or every sixth	Classification of		(those 65 and	missing data	suggests study		
		day. There was no	Diseases, 9th Revision		older) of	did not depend	was free of		
		information about	(ICD-9) codes,		cardiovascular	on air pollution	selective		
		missing data.	emergency		disease and	levels.	report.		
			hospitalizations for the		respiratory				
			elderly (those 65 and		diseases.				
			older) data were divided						
			into cardiovascular						
			disease and respiratory						
			categories.						

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
54	Ostro et	The model calculations	Deaths were assigned	ge, race, marital	Data obtained for	There was no	There was	The authors	No other
	al. 2015b	track the mass and	codes based on the	status, smoking	a cohort of	information on	insufficient	declare they	potential
		concentrations of the PM	International	status, pack-years	female teachers	the rate of lost	information	have no	sources of
		constituents in particle	Classification of	of smoking,	≥30 years old.	follow up.	about	actual or	bias
		diameters ranging from	Diseases, 10th Revision	secondhand smoke			selective	potential	identified.
		0.01 to 10μm through	(ICD-10) for the	exposure, body			outcome to	competing	
		calculations that describe	following outcomes:	mass index,			judge for low	financial	
		emissions, transport,	all-cause deaths	lifetime physical			risk, but	interests.	
		diffusion, deposition,	excluding those with an	activity, alcohol			indirect		
		coagulation, gas- and	external cause	consumption,			evidence that		
		particle-phase chemistry,	(A00–R99),	average daily			suggests study		
		and gas-to-particle	cardiovascular deaths	dietary intake of			was free of		
		conversion. The	(I00–I99), Ischemic heart	fat, calories,			selective		
		University of California	disease deaths (I20–I25),	menopausal status,			report.		
		Davis/California Institute	and pulmonary deaths	family history of					
		of Technology model was	(C34, J00–J98).	myocardial					
		used to estimate		infarction, stroke,					
		ground-level		use of blood					
		concentrations of 50 PM		pressure					
		constituents over the		medication,					
		major population regions		aspirin; living					
		in California.		conditions					

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
				(income, income					
				inequality,					
				education,					
				population size,					
				racial composition,					
				unemployment).					
		Probably Low	Low	Probably High	Low	Probably Low	Probably Low	Low	Low
55	Gan et al.	Using high spatial	The study used	Individual-level	Data obtained for	During the	There was	The authors	No other
	2013	resolution land use	International Statistical	covariates: age,	a cohort of	4-year	insufficient	declare they	potential
		regression models to	Classification of	sex, preexisting	people (45-85	follow-up	information	have no	sources of
		estimate residential	Diseases, 9th Revision	comorbid	years old)	period, 38,377	about	actual or	bias
		exposure to traffic-related	(ICD-9) codes 490–492	conditions; and	registered with	(8%) subjects	selective	potential	identified.
		air pollutants including	and 496 or 10th Revision	neighborhood	the provincial	were lost to	outcome to	competing	
		black carbon. During the	(ICD-10) codes J40–J44	socioeconomic	health insurance	follow-up	judge for low	financial	
		5-year exposure period,	to identify COPD cases	status (SES).	plan. Study	because of	risk, but	interests.	
		individual exposures to	during the 4-year		provided total	moving out of	indirect		
		ambient air pollutants	follow-up period.		number of	the province or	evidence that		
		were estimated at each			subjects along	dying from	suggests study		
		person's residential postal			with those lost	other diseases.	was free of		
		code centroid using land			during the		selective		
		use regression models.			follow-up period.		report.		

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
56	Hvidtfeldt	The PM, NO ₂ , BC, and	Participants who died	Age, sex,	Data obtained for	There was no	There was	The authors	No other
	et al. 2019	O ₃ concentrations at	from external causes such	educational	a cohort of men	information on	insufficient	declare they	potential
		residential addresses of	as injuries, accidents and	attainment,	and women aged	the rate of lost	information	have no	sources of
		the cohort members were	suicides (International	occupational	50-64 years	follow up.	about	competing	bias
		derived by a	Classification of	status, marital	residing in the		selective	financial	identified.
		high-resolution	Diseases, 10th	status, smoking	areas of		outcome to	interests.	
		dispersion modelling	Revision-ICD-10 codes	(status, intensity,	Copenhagen and		judge for low		
		system which	S–Z) were censored at	and duration),	Aarhus.		risk, but		
		incorporates	date of death. In addition,	environmental			indirect		
		contributions from local,	the study investigated	tobacco smoke			evidence that		
		urban, and regional	cardiovascular (ICD10	(ETS), alcohol			suggests study		
		sources of precursors to	codes I00–I99) and	consumption, body			was free of		
		PM, NO ₂ , BC, and O ₃ .	respiratory (ICD10 codes	mass index, waist			selective		
			J00–J99 and C34)	circumference,			report.		
			subgroups of mortality.	fruit consumption,					
				vegetable					
				consumption,					
				physical activity;					
				neighborhood					
				level					
				socioeconomic					
				status (SES).					

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
57	Thurston	The mean concentrations	More than 99% of known	Active smoking	Data obtained for	The analytic	There was	No	No other
	et al. 2016	of PM _{2.5} mass and trace	deaths were assigned a	and former	a cohort of	cohort included	insufficient	competing	potential
		constituents were	cause using the	smoking, passive	persons at least	445,860	information	financial	sources of
		obtained from U.S.	International	smoke exposure,	30 years of age,	participants,	about	interests.	bias
		Environmental Protection	Classification of	possible workplace	in households	with 34,408	selective		identified.
		Agency Air Quality	Diseases, 9th and 10th	exposure to PM,	including	Ischemic heart	outcome to		
		System. These PM _{2.5}	Revision (ICD-9 codes	occupational	someone at least	disease deaths	judge for low		
		constituent data were	410–414; ICD-10 codes	dirtiness index,	45 years of age	(of a total of	risk, but		
		analyzed to derive	I20–I25).	marital status,	and resided in all	157,572 deaths	indirect		
		estimates of source		education, BMI	50 states, the	from all	evidence that		
		apportioned PM _{2.5} mass		and BMI ² ,	District of	causes)	suggests study		
		exposure concentrations		consumption of	Columbia, and	occurring	was free of		
		using the absolute		beer, wine, and	Puerto Rico.	during	selective		
		principal component		other alcohol,		follow-up.	report.		
		analysis (APCA) PM _{2.5}		quintile of dietary					
		source apportionment		fat consumption,					
		method.		quintile of					
				combined dietary					
				vegetable, fruit,					
				fiber consumption;					
				Six ecologic					
				covariates.					

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
58	Yang et al.	Land use regression	Deaths were coded	Age at entry,	Data obtained for	There was no	There was	The authors	No other
	2018	models were derived	according to the	gender, individual	a cohort of	information on	insufficient	declare they	potential
		from street level	International	smoking status,	people who were	the rate of lost	information	have no	sources of
		measurements collected	classification of Diseases,	body mass index	older than or	follow up.	about	actual or	bias
		during two sampling	10th Revision (ICD-10;	(BMI), physical	equal to 65 years		selective	potential	identified.
		campaigns conducted in	WHO 2010) including	activity, education	old.		outcome to	competing	
		2014 and 2015.	natural cause mortality	level and monthly			judge for low	financial	
			(A00–R99), overall	expenses;			risk, but	interests.	
			cardiovascular disease	percentage of			indirect		
			(I00–I99) and overall	participants who			evidence that		
			respiratory disease	were equal to or			suggests study		
			(J00–J47 and J80–J99).	older than 65 years			was free of		
			Subcategories included	old, percentage of			selective		
			Ischemic heart disease	participants whose			report.		
			(IHD) (I20–I25),	educational level					
			cerebrovascular disease	was higher than					
			(I60–I69), Pneumonia	secondary school,					
			(J12–J18) and chronic	average income					
			obstructive pulmonary	per month and					
			disease (COPD) (J40–I44	percentage of					
			and I47).	smokers.					

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	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	selective	potential	identified.
			Classification of	socioeconomic	follow-up period.	out of the	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			418,826	was free of		
			responsible diagnosis) for			(9 _{2.5} %)	selective		
			a hospital admission in			subjects at the	report.		
			the hospitalization			end of			
			database. A coronary			follow-up.			
			heart disease death is a						
			death record with						
			coronary heart disease as						
			the cause of death in the						
			provincial death						
			registration database.						

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
60	De	Used black smoke (BS)	The study obtained	Individual-level	Data obtained for	There was no	There was	No	No other
	Kluizenaa	as an indicator of EC	information on the	covariates: age,	a cohort of	information on	insufficient	competing	potential
	r et al.	concentrations. Derived	incidence of	gender, marital	27,070	the rate of lost	information	financial	sources of
	2013	background EC	hospital-based Ischemic	status, education,	non-institutionali	follow up.	about	interests.	bias
		concentrations from BS	heart disease	smoking, alcohol	zed subjects.		selective	identification is selective selective selective solutions to study for low risk, but sindirect sevidence that	
		measured at two regional	(International	use, physical			outcome to	interests. bias identified ow hat tudy	
		monitoring sites. Local	Classification of Diseases	activity, body mass			judge for low	lective identified to to to dge for low k, but direct idence that ggests study as free of	
		traffic-related EC	[ICD9] 410-414) and	index, living			selective identified outcome to		
		emission contributions	cerebrovascular disease	conditions			indirect		
		were estimated based on	(ICD9 430-438) in the	(employment			evidence that		
		fuel-specific EC content	study population.	status, financial			suggests study		
		of exhaust PM ₁₀		problems).			was free of		
		emission. Used the					selective		
		traffic-related EC					report.		
		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 .							

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
61	Vedal et	The exposure estimation	All outcomes were	Individual-level	Data obtained for	There was no	There was	No financial	No other
	al. 2013	were used the national	reported via questionnaire	covariates: age,	a cohort of	information on	insufficient	interests.	potential
		spatial model predictions	and assessed via	body mass index,	postmenopausal	the rate of lost	information		sources of
		and secondary exposure	physician-adjudicator	smoking status,	women.	follow up.	about		bias
		measures of citywide	review of medical records	cigarettes smoked			selective		identified.
		average exposures and	following established	per day and years			outcome to		
		distance to major	protocols.	of smoking,			judge for low		
		roadways.		systolic blood			risk, but		
				pressure, history of			indirect		
				hypertension,			evidence that		
				hypercholesterole			suggests study		
				mia, history of			was free of		
				diabetes,			selective		
				education,			report.		
				household income					
				level, and race.					

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		High	Low	Probably Low	Low	Low	Probably Low	Low	Low
62	Rahmatini	BC were collected from	Daily non-accidental	Models adjusted	Study included	Daily counts	There was	The authors	No other
	a et al.	two monitors (Sharif and	deaths were obtained	for time,	all daily	for death were	insufficient	of this	potential
	2021	Setad) with data recorded	from Ministry of Health	temperature,	non-accidental	obtained, so	information	article	sources of
		at 5 min intervals. BC	and Medical Education	relative humidity,	deaths from	likely have all	about	declare that	bias
		measurements began	database. The causes of	atmospheric	Ministry of	outcome data.	selective	they have	identified.
		from March 2017 to	death were coded	pressure, PM2.5	Health and	However, any	outcome to	no conflict	
		August 2017. But the	according to the	data, Day of week	Medical	potential errors	judge for low	of interests.	
		gaseous pollutant at the	International	(DOW) and public	Education	or missing data	risk, but		
		Setad site were unreliable	Classification of Disease	holidays.	database from	did not depend	indirect		
		and models utilizing the	(10th revision—ICD-10).		March 2017 to	on air pollution	evidence that		
		2-site data were			August 2017.	levels.	suggests		
		unsatisfactory. So, only					study was		
		the Sharif data were used.					free of		
							selective		
							report.		

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
63	Liu et al. 2021b	Annual county-level exposures of PM2.5 and its constituents for each participant were assessed by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.	The three cardiovascular events as health outcomes: 1) total cardiovascular disease, including but not limited to hypertension and stroke; 2) hypertension; 3) stroke were defined according to the Disease Classification Codebook for Chinese Family Panel Studies.	Model adjusted for age, gender, education level (illiteracy, primary to middle school, and high school or above), household income (RMB, strata of ≤ 15,000, 15,000 − 40,000, and 40,000 +, grouped according to the upper and lower quartiles), urbanicity (urban/rural, defined by CFPS participants' home addresses).	All of participants were drawn from the China Family Panel Studies (CFPS) launched by Peking University Institute of Social Science Survey (ISSS) in 2010, an ongoing national longitudinal survey of social-demograp hy in China.	The cohort included 14,331 adults who completed three waves of follow-up.	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.

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
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
	al. 2021	gridded at a resolution of	asthma cases were	parity, child sex,	data on singleton	information on	insufficient	declared	potential
		approximately 1-km2	identified according to	breastfeeding	live births that	the rate of lost	information	that there is	sources of
		was derived using	International	status at the time	occurred	follow up.	about	no conflict	bias
		multiple satellite-based	Classification of Diseases	of discharge,	between April 1st		selective	of interest.	identified.
		retrievals of aerosol	[ICD]-10: J45.	maternal smoking	2006 and March		outcome to		
		optical depth in		during pregnancy,	31st 2014 in the		judge for low		
		combination with a		maternal atopy,	Province of		risk, but		
		chemical transport model,		gestational age and	Ontario, Canada.		indirect		
		and enhanced through		birth weight.	Mother-infant		evidence that		
		statistical incorporation			pair data were		suggests		
		of ground- based			obtained from		study was		
		observations (including			the Better		free of		
		BC).			Outcomes		selective		
					Registry &		report.		
					Network				
					(BORN) Ontario,				
					a province wide				
					birth registry that				
					captures				
					perinatal health				
					information.				

odins et 1. 2020	Probably Low The study used the validated, time-dependent,	Probably Low Cardiovascular outcomes in the HNR Study were	Probably Low Model adjusted for	Low The study used	Probably Low	Probably Low	Low	Low
	validated, time-dependent,		Model adjusted for	The study used				
	three-dimensional European Air Pollution Dispersion chemistry transport model (EURAD) to estimate the exposure to EC.	determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records.	age, sex, individual and neighborhood SES, BMI, nighttime traffic noise exposure and lifestyle factors: smoking, alcohol consumption, physical activity and nutritional pattern.	baseline (2000–2003) and 14 years follow-up data from the German HNR Study, an ongoing population-based prospective cohort study.	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 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.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably High	Low	bin bias outcome data reporting interest W Low Probably Low Low Cluded Daily counts for emergency insufficient declare no information about interest. Exp department information conflict of about interest. Exp department information about interest. Exp department information conflict of interest. Exp department information about interest. Exp department information conflict of interest. Exp department information about interest. Exp department information conflict of interest. Exp department information about interest. Exp department information conflict of interest. Exp department information interest. Exp department information conflict of interest. Exp department information information conflict of interest. Exp department information interest. Exp department information conflict of interest. Exp department information information interest.	Low		
66	Kovačević	The daily average	The data of emergency	Model adjusted for	Study included	ow Low Probably Low Low Included Daily counts at a of for emergency department information about selective so likely have all outcome to get Health either any potential exercise or missing data are) in Užice st July Low Included Daily counts There was insufficient declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest. The authors declare no conflict of interest.	No other		
	et al. 2020	concentration of BC were	department (ED) visits	seasonality,	all the data of	for emergency	insufficient	declare no	potential
		collected from three	for allergic asthma were	long-term trends,	emergency	department	information	conflict of	sources of
		automatic ambient air	robably Low Low Probably High Low ly average tration of BC were department (ED) visits for allergic asthma were collected from the Užice the alth Centre, either located in Užice, and Kosjerić. The data of emergency department (ED) visits for allergic asthma were collected from the Užice the monitoring Located in Užice, and Kosjerić. The data of emergency department (ED) visits for allergic asthma were collected from the Užice themperature, humidity, air pressure, air pollutants and collected to the Užice asthma were care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice. International Classification of Diseases, 10th revision, codes were used in the	department (ED)	(ED) visits	about	interest.	bias	
		Probably Low 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. Probably Low The daita of emergency department (ED) visits for allergic asthma were collected from the Užice (International Realth Centre, either from the EDs (International Realth Centre) 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	Health Centre, either	humidity, air	visits for allergic	were obtained,	selective		identified.
		stations located in Užice,	Low Low Probably High The data of emergency department (ED) visits for allergic asthma were collected from the Užice Health Centre, either nu Užice, from the EDs (ambulances or home ed care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice. Tormation International codes were used in the diagnosis of allergic asthma or asthma with coexisting allergic rhinitis (AR). Probably High Model adjusted for Studies seasonality, all the seasonality, all the seasonality, the seasonality, all the seasonality.	asthma were	so likely have	outcome to			
		Probably Low 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 ard 30th June 2014. There was no information about missing data. D coding the desired concentration are desired as as coding and a concentration are desired as a coding as a coding are desired as a coding as a coding are desired as a coding are desired as a coding as a coding are desired as a coding as a coding are desired as a coding as a codin	(ambulances or home	pollutants and	collected from	all outcome	judge for low		
		BC were measured	care) in Užice, Sevojno,	pollens.	the Užice Health	data. However,	risk, but		
		between 1st July 2012	and Kosjerić or from a	Probably High Low Low Probably Low Low Model adjusted for seasonality, all the data of humidity, air pressure, air pollutants and pollens. Centre, either from the EDs (ambulances or home care) in the Užice, Sevojno, and Kosjerić or from a general hospital in Užice Probably High Low Low Probably Low Low Daily counts for emergency department (ED) Low Indicate Probably Low Low Indicate Probably Low Low Indicate Probably Low Low Indicate Probably Indic					
		and 30th June 2014.	general hospital in Užice.		Selection bias Low Low Probably Low There was all the data of emergency department (ED) visits for allergic asthma were collected from the Užice Health (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice during 1st July 2012 to 30th Study included Low Probably Low Probably Low Probably Low There was interest The authors declare no pote insufficient information conflict of sour interest. No declare no pote insufficient indirect errors or evidence to selective outcome to judge for low the Užice Health data. However, risk, but indirect evidence that suggests study was free of selective report.				
		There was no information	International		Probably High Low Low Daily counts for emergency all the data of emergency department (ED) (ED) visits about interest. Indicate the state of the Užice Health (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice during 1st July 2012 to 30th Daily counts There was insufficient declare no conflict of insufficient information conflict of insufficient ins				
		about missing data.	Probably Low Low De daily average Ine data of emergency department (ED) visits all the data of department (ED) visits department (ED) visits all the data of department (ED) visits department (ED) visits department (ED) department (ED) department (ED) visits for allergic asthma were collected from the EDs department (ED) department (ED) department (ED) visits for allergic asthma were asthma were collected from department (ED) visits for allergic asthma were collected from department (ED) visits for allergic asthma were collected from all outcome all outcome all outcome all outcome data. However, ri from the EDs data department (ED) visits department (ED) visits department (ED) visits department (ED) visits all the data of department (ED) visits os likely have or all outcome all outcome all outcome all outcome data. However, ri from the EDs data However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits os likely have or all outcome all outcome data. However, ri department (ED) visits or asthma were collected from all outcome all outcome of the Užice Health centre, either from the EDs comercial however, ri department (ED) visits or asthma were asthma were collected from all outcome all outcome of the Užice, Sevojno, and Kosjerić or from the EDs comercial however, ri didnot depend on air pollution on air poll	study was					
			Diseases, 10th revision,		Užice, Sevojno,	on air pollution	free of		
			codes were used in the		and Kosjerić or	levels.	selective		
			diagnosis of allergic		from a general		report.		
			asthma or asthma with		hospital in Užice				
			coexisting allergic rhinitis		during 1st July				
			(AR).		2012 to 30th				
					June 2014.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
67	Hasslöf et	BC levels were modelled	The outcomes were	Model adjusted for	In the	Of these, 224	There was	The authors	No other
	al. 2020	using EnviMan (Opsis	plaque presence and	age, sex, air	cardiovascular	were missing	insufficient	declare that	potential
		AB, Sweden) by the	CIMT of the right carotid	pollutant,	subcohort of the	data on plaque	information	they have	sources of
		Environmental	artery, which were	education level,	MDCS cohort,	and 20 on	about	no known	bias
		Department of Malm"o.	assessed by ultrasound	smoke score,	6031 participants	Probably Low Probably Low Low I I The authors declare that information about selective outcome to included in the plaque analyses in the alyses and in the alyse and in	identified.		
		The program uses a	examination B-mode	apoB/apoA1 ratio,	who had a				
		Gaussian dispersion	ultrasonography,	use of lipid	residential	Hence, the	Probably Low Probably Low Low Low Of these, 224 There was insufficient ata on plaque information about no known bias identify espectively. Hence, the judge for low unber of risk, but personal articipants indirect relationship evidence that suggests are 5807 and in the CIMT free of influence the work report. Probably Low		
		model (AERMOD)	conducted by trained and	lowering drugs,	address within	Probably Low Probably Low The authors were missing insufficient and 20 on about selective outcome to number of participants included in the plaque analyses were 5807 and in the CIMT free of the competition of the competition in the CIMT analyses 6011. Probably Low Probably Low Low The authors declare that pot they have no known biast of they have no known competing in the competing independent of they have no known biast or prespectively. Outcome to judge for low interests or personal relationship included in the evidence that suggests have appeared to influence the work report.			
		combined with an	certified sonographers.	living alone,	the air pollution	participants	indirect	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	
		emission database for the		cardiovascular	modelling area.	included in the	evidence that	s that could	
		county of Scania in		heredity, diabetes	Of these, 224	plaque analyses	suggests	have	
		Sweden.		mellitus, waist hip	were missing	were 5807 and	study was	reporting interest Debably Low Low Low Low Ere was The authors ufficient declare that formation they have no known ective competing financial lifect relationship dence that speeds to be of influence ective the work fort.	
				ratio, physical	data on plaque	Low Probably Low Probably Low In the ardiovascular who had a esidential dates within me air pollution modelling area. Of these, 224 were missing atata on plaque in the CIMT analyses 6011. Low Probably Low Probably Low Low Interest of the areporting insufficient information and color they have sour about no known bias selective competing iden interests or risk, but personal included in the plaque analyses were 5807 and in the CIMT analyses overe 5807 and in the CIMT interests or protectively. Low Probably Low Probably Low Low Interest or the authors declare that pote they have sour no known bias competing incompeting include for low risk, but personal interests or relationship state could suggests study was appeared to influence they were of selective report. Low Probably Low Interest of the authors declare that pote of information about no known bias competing incompeting interest or respectively. The sumber of included in the old aque analyses overe 5807 and in the CIMT interest or pote of influence they are possible to the work report.			
				activity, alcohol	bably Low I adjusted for ex, air ant, subcohort of the tion level, apoA1 ratio, residential alone, rowscular subcaular alone, rowscular subcaular alone, rowscular subcaular alone, rowscular alone, rowscular subcaular alone, rowscular subcaular and 20 on alone, rowscular alone, rowscular alone, rowscular and 20 on alone, rowscular and 20 on alone, rowscular alo	the work			
				Probably Low	reported in				
							this paper.		
				level in residential	participants				
				area, systolic blood	included in the				
				pressure and being	plaque analyses				
				Sweden.	the CIMT				
					analyses 6011.				

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably High	Probably Low	Probably High	bably High Low Low Probably Low Low I adjusted for all patients treated at the return trends, rature and the humidity. Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY interest and count outcome data reporting interest interests. Low Probably Low Low There was insufficient insufficient insufficient information about no competing interests.	Low	Low		
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
	al. 2019b	routine air quality	Cardiac Catheterization	seasonality,	all patients	for all patients	insufficient	declare that	potential
		monitoring site operated	Laboratory (Cath Lab) at	long-term trends,	treated at the	were obtained,	information	they have	sources of
		by the New York State	URMC in Rochester, NY	temperature and	Cardiac	so likely have	about	no	bias
		Department of	Probably High Probably Low Probably High Low Low Probably High Were collected from a ine air quality Laboratory (Cath Lab) at Laboratory (Cath Lab) at he New York State artment of within 15 miles of the servation servation 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 Probably High Low Low Probably High Low Selection bias outcome data relative high probably High Low Daily counts for all patients insure seasonality, all patients treated at the were obtained, info all patients treated at the were obtained, so likely have abore all outcome all outcome all outcome all outcome data. However, outcome data The Cardiac So likely have abore all outcome selection in Rochester were included. American College of Cardiology (ACC)/American Heart Association (AHA) guidelines were used at the time of Cath Lab	selective	competing	identified.			
		Environmental	Probably High Probably Low Probably High Low Daily counts of quality agsite operated that of ental within 15 miles of the pollution monitoring sly throughout period included. American College of Cardiology (ACC)/American Heart at a. Association (AHA) guidelines were used at the time of Cath Lab admission to diagnose	outcome to	interests.				
		Probably High 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. Probably Low Probably Low Probably High All patients treated at the Cardiac Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY temperature and relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative humid relative humid relative humid seasonality, long-term trend temperature and relative humid relative		Lab) at URMC	any potential	judge for low			
		continuously throughout	station in Rochester were		in Rochester, NY	errors or	risk, but		
		the study period	included. American		for STEMI	missing data	indirect		
		(2005–2016). There was	College of Cardiology		throughout the	did not depend	evidence that		
		no information about	(ACC)/American Heart		study period	on air pollution	suggests		
		missing data.	Association (AHA)		(2005–2016).	levels.	study was		
			guidelines were used at				free of		
		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. BC were collected from a routine air quality BC were collected from a routine air quality Cardiac Catheterization Laboratory (Cath Lab) at long-term trends, treated at the were of temperature and relative humidity. Cardiac Catheterization Laboratory (Cath Lab) at long-term trends, treated at the long-term trends, treated at the were of temperature and relative humidity. Catheterization Laboratory (Cath Lab) at URMC any pot in Rochester, NY for STEMI throughout the study period (2005–2016). There was no information about missing data. Association (AHA) guidelines were used at the time of Cath Lab admission to diagnose		selective					
		Department of for Environmental with Conservation continuously throughout the study period (2005–2016). There was no information about missing data. Conservation pollocation includes the study period (AC missing data). Assignificant continuous properties and the study period (AC missing data).	admission to diagnose				report.		
			STEMI.						

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
69	Ljungman	Based on detailed	The International	Model adjusted for	The study	The study used	There was	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	information	have no	sources of
		high-resolution	(ICD-9) codes 410–414	smoking status,	two cohorts from	comprehensive	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	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 Um	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.	Probably Low Model adjusted for sex, calendar year, including status, alcohol consumption in Stockholm and Umeå, physical activity, marital status, socioeconomic index by occupation, education level, occupation status, and mean neighborhood individual income in persons of working age by Small Areas for	total, 114,758	follow-up for	evidence that		
		other sources in		socioeconomic	individuals were	our outcomes	suggests		
		Gothenburg, Stockholm,		index by	included from all	of interest.	study was		
		and Umeå.		occupation,	study areas.	Missing	free of		
				education level,		information for	selective		
				occupation status,		variables ≤	report.		
				and mean		5% not			
				neighborhood		specified.			
				individual income					
				in persons of					
				working age by					
				Small Areas for					
				Market Statistics.					

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
70	Liu et al.	Annual mean	COPD was defined by	Model adjusted for	The study used	From a total of	The authors of the authors of the authors of the about of the selective of the authors of the about of the selective of the about of the selective of the authors of the about of the authors of the auth	No other	
	2021a	concentrations of BC for	following the principal	age, sex, smoking	data from three	106,727	insufficient	declare that	potential
		2010 were estimated at	diagnosis of International	status, smoking	cohorts within	participants	information	they have	sources of
		the study participants'	Classification of	duration, smoking	the ELAPSE	with complete	about	no known	bias
		baseline residential	Diseases, 9th Revision	ion intensity, body-mass index, available exposure data, outcome to financia interests employment status, educational level and project with air pollution exposure data, outcome to financia interests excluded 633 risk, but personal participants with COPD at evidence that status status air pollution exposure data, outcome to financia interests risk, but personal indirect relations with COPD at evidence that status status.	competing	identified.			
		addresses, using	(ICD-9) codes 490–492,	status, smoking duration, smoking intensity, project with air pollution selective project with air pollution selective competing outcome to marital status, information on employment status, educational level and area-level annual status, infollow-up time is status, educational duration status, educational follow-up time is status, educational duration, smoking the ELAPSE with complete about no known selective competing outcome to financial judge for low interests or excluded 633 risk, but personal indirect relationship evidence that suggests have	financial				
		standardized	and 494–496, or ICD-10	egnosis of International assification of duration, smoking seases, 9th Revision about seases, 9th Revision body-mass index, ad 494–496, or ICD-10 des J40–44. COPD hospital level and area-level annual year income. Status, smoking the ELAPSE project with available available information on the study judge for love excluded 633 participants indirect evidence that suggests study was free of with missing information.	judge for low	interests or			
		Europe-wide hybrid land	codes J40–44.	g the principal s of International status, smoking action of codes 490–492, apply 6. 496, or ICD-10 0—44. The principal status, smoking duration, smoking intensity, body-mass index, employment status, educational level and area-level annual year income. The principal status, smoking data from three cohorts within the ELAPSE project with air pollution selective about status, education and discharge diagnoses. Mean follow-up time is participants with COPD at status, education and follow-up time is participants with missing information on report. The principal status, information with complete about selective about status, outcome to project with air pollution exposure data, outcome to provide for excluded 633 risk, but indirect shading area-level annual status, educational discharge area-level annual per income. The principants information on the study indirect evidence suggests study was participants free of with missing information on report.	risk, but	personal			
		use regression (LUR)		status, educational	discharge	From a total of e 106,727 insufficient declare that participants information air pollution exposure data, the study judge for low excluded 633 participants indirect e is baseline and se is baseline and 7,586 study was participants free of information on report. The authors declare that potential sources of bias interests of potential sources of bias identified. No other potential sources of bias identified.			
		models. The LUR model		level and	diagnoses. Mean	with COPD at	evidence that	The authors declare that they have sources of no known competing financial interests or personal relationship s that could have appeared to influence the work reported in	
		utilized routine		area-level annual	follow-up time is	baseline and	suggests	no known competing financial interests or personal relationship s that could have appeared to influence the work reported in	
		monitoring data from the		year income.	16.6 years.	7,586	re data, outcome to financial interests or risk, but personal relationship evidence that suggests have study was appeared to influence issing selective the work reported in		
		European Environment				participants	ticipants information about no known pollution selective competing financial interests or pluded 633 risk, but personal ticipants indirect relationship selicine and suggests study was appeared to ticipants free of influence the missing selective the work permation on report.		
		Agency (EEA) AirBase			cohorts within participants information they have about no known bias project with air pollution selective competing available exposure data, information on the study judge for low interests or excluded 633 risk, but personal discharge participants indirect relationship diagnoses. Mean follow-up time is baseline and suggests have 16.6 years. They have sources of they have bias sources of they have to have sources of they have to have sources of they have they have to have they have they have to have they have they have to have they have th				
		for PM2.5, NO2, and O3,		marital status, employment status, educational level and area-level annual year income. Marital status, education on comployment status, educational level and area-level annual year income. 16.6 years. 16.					
		and ESCAPE monitoring				confounders.		this paper.	
		data for BC as the							
		dependent variable. BC							
		was measured by the							
		reflectance of PM2.5							
		filters and expressed in							
		absorbance units.							

Supplemental material

					Reaso	ns for downgrading							Rea	sons for upgrading				Final
Evidence	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	В1	Rationale	B2	Rationale	В3	Rationale	Overall	certainty
Acute effects of BC/EC on CVD in PM _{2.5} -unadjusted model	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	0	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	-1	Low
Acute effects of BC BC/EC on CVD in PM _{2.5} -adjusted model	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	0	Confounders would shift the RR in both directions	0	Evidence of increase in risk with increasing exposure	0	Moderate
Chronic effects of BC/EC on CVD in $PM_{2.5}$ -unadjusted model	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	0	Confounders would shift the RR in both directions	0	No evidence of a clear increasing risk with exposure	0	Moderate

Abbreviations: BC: Black carbon; EC: Elemental carbon; CVD: cardiovascular diseases; RES: respiratory diseases; IHD: ischemic heart diseases; PI: prediction interval; CI: confidence interval. A1 = limitations in studies (risk of bias); A2 = indirectness; A3 = inconsistency; A4 = imprecision; A5 = publication bias; B1 = large RR; B2 = all confounding decreases observed RR; B3 = concentration-response gradient.

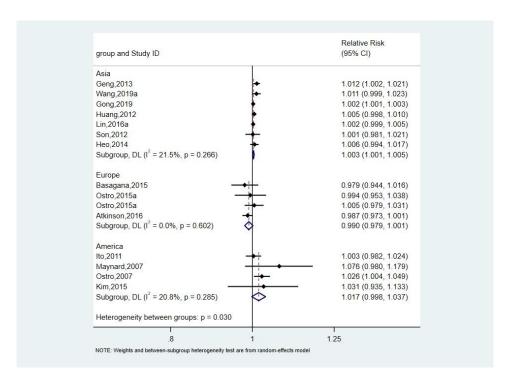


Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

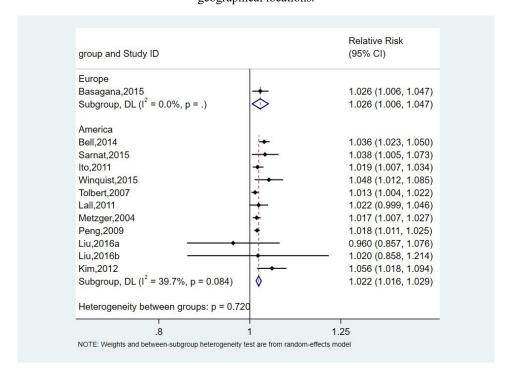


Figure S2 Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

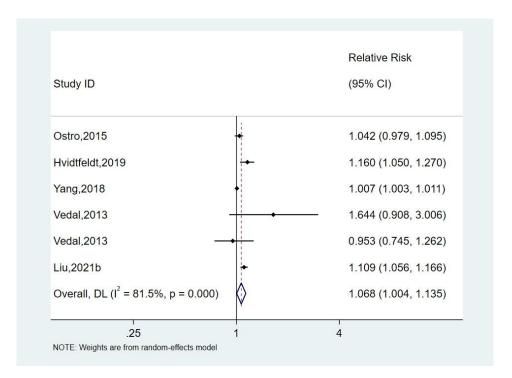


Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.

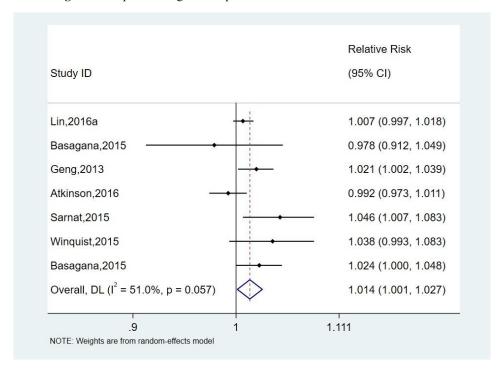


Figure S4 Impact of short-term exposure to BC/EC on cardiovascular diseases in the $PM_{2.5}$ -adjusted model.