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Is short-term and long-term exposure to black carbon associated with cardiovascular and respiratory diseases? A systematic review and meta-analysis based on evidence reliability

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ABSTRACT

Objective Adverse health effects of fine particles (particulate matter$_{2.5}$) have been well documented by a series of studies. However, evidences on the impacts of black carbon (BC) or elemental carbon (EC) on health are limited. The objectives were (1) to explored the effects of BC and EC on cardiovascular and respiratory morbidity and mortality, and (2) to verified the reliability of the meta-analysis by drawing p value plots.

Design The systematic review and meta-analysis using adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and p value plots approach.

Data sources PubMed, Embase and Web of Science were searched from inception to 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% CI. 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/m^3 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.

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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 thermo-optical method.[1 2] Although the measurement methods are different, BC and EC are often considered interchangeable. BC is mainly emitted from traffic and combustion-related sources and is a measured component of the PM. The adverse health effects of PM, especially PM$_{2.5}$, are well documented. In 2017, a total of 2.94 million deaths resulted from ambient PM worldwide.[3–5] PM$_{2.5}$ is composed of various constituents, in which some of them are more toxic and hypothesised as the main cause of the adverse effects of PM$_{2.5}$. A growing body of studies indicates a potential role of BC among these more toxic constituents.[6 7] In addition, some reviews demonstrated that BC is a better indicator of adverse effects of PM from combustion sources according to robust associations from epidemiological studies.[8 9] The underlying pathological mechanisms of BC include oxidative stress, inflammation and gene mutations.[10–12]

Due to its association with adverse health, the number of studies exploring the effects of BC on cardiorespiratory diseases has rapidly increased in recent years. Cardiovascular and respiratory diseases are common diseases worldwide, with a heavy disease burden and major implications for clinical practice and public health. The global burden of disease study 2017 indicated that cardiovascular and respiratory-related death ranked first and third respectively among non-communicable diseases.[4] Health effects of acute and chronic exposure to BC have been widely reported. Despite that there is some epidemiological evidence that BC was associated with cardiorespiratory diseases, in other studies, no statistically effects were observed.

The reliability of air quality epidemiological studies is often poor, with a serious lack of reproducibility of published findings.[13]

A lack of reproducibility in epidemiological studies can be attributed to many factors, but p-hacking is a common issue. If researchers run a regression with and without outliers, with and without a covariate, with one and then another dependent variable, then false positive results are much more likely to be reported. There can be a selective reporting problem (compute many tests and selectively report small p values), which is referred to p-hacking.[14] When a study examines many questions, tests numerous statistical models and does not perform multiple testing statistical corrections, p hacking is referred to as multiple testing and multiple modelling.[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 short-term 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 J00–J99, 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:

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

Two studies did not show the overall risk, while stratified risk estimates by age and location were reported.[21 22] In this case, the stratified estimates were pooled. One study presented the estimates of both morbidity and mortality, which were combined in the overall analysis.[23] In addition, if the same cohort data were 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:

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

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 $PM_{2.5}$ is a potential confounder in assessing the health effects of $PM_{2.5}$ constituents.[7] For overall and outcome analysis, $PM_{2.5}$-adjusted estimates and $PM_{2.5}$-unadjusted estimates in the models were combined, respectively where more than three estimates were available. Regarding the subgroup analysis, $PM_{2.5}$-unadjusted estimates were analysed, while $PM_{2.5}$-adjusted estimates were not presented due to the limited number of included studies. Moreover, primary data of the included studies could not be obtained, hence it was impossible to evaluate whether the same patients were repeatedly included across multiple studies. Therefore, the sensitivity analysis was performed on all age populations to investigate the robustness of the aggregation results by the removal of studies with partial temporal overlap from the same geographical location. Most of the included studies 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:

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

$$Z = \ln RR/SE$$

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

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

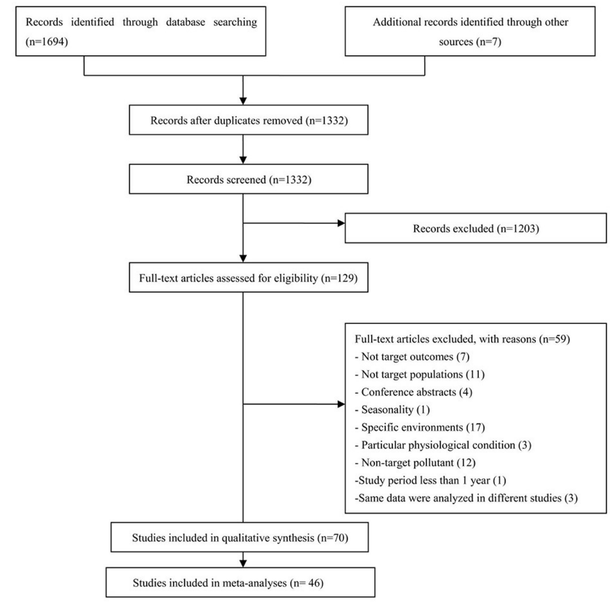

Figure 1 Flow diagram of hliterature screening process.

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 µg/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 µg/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 µg/m3, 95% CI 1.006 to 1.016), and then diminished on lag 1 (RR 1.005 per 1 µg/m^3, 95% CI 1.002 to 1.008) and lag 2 (RR 1.002 per 1 µg/m^3, 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 to 1.001) (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

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

	$PM_{2.5}$-unadjusted model				$PM_{2.5}$-adjusted model				
Subgroup analysis	**No of studies**	**No of estimates**	**Relative Risk (95% CI)**	**I^2**	**Egger regression test (p value)**	**No of studies**	**No of estimates**	**Relative Risk (95% CI)**	**I^2**
Cardiovascular diseases									
Age									
All population	20	22	1.008 (1.004 to 1.012)	64.40%	0.007	6	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)	—	—	—	—	—	—
Sensitive analysis on study of partial temporal overlap from the same geographical location	16	16	1.006 (1.002 to 1.010)	60.00%	0.020	—	—	—	—
≥65 years	5	6	1.016 (1.004 to 1.028)	87.40%	—	—	—	—	—
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	14	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	5	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)	90.30%	0.449	—	—	—	—
≥65	3	4	1.038 (1.006 to 1.071)	82.90%	—	—	—	—	—
Outcome									
Morbidity	10	10	1.012 (0.993 to 1.031)	91.80%	0.671	3	5	0.996 (0.987 to 1.004)	0
Mortality	10	11	1.013 (0.997 to 1.030)	66.40%	0.328	3	3	1.017 (0.985 to 1.050)	48.30%

BC/EC, black carbon/elemental carbon; PM, particulate matter.

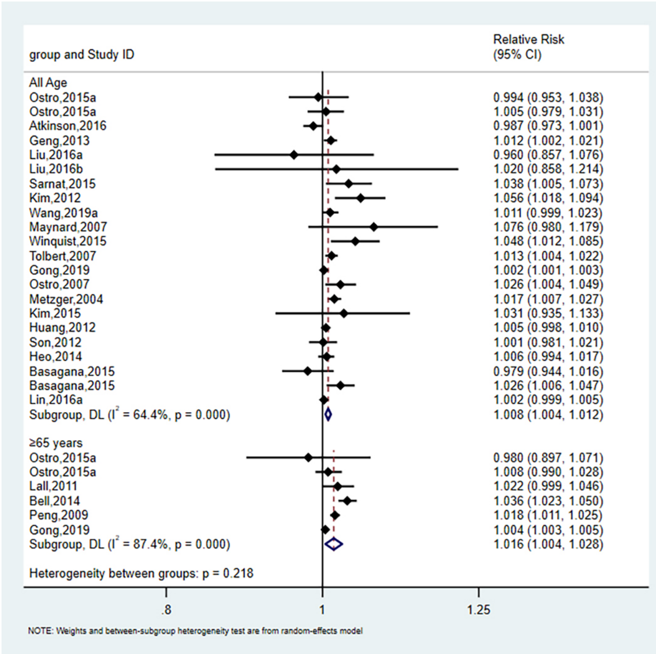

Figure 2 Impact of short-term exposure to BC/EC on cardiovascular diseases in the $PM_{2.5}$-unadjusted model. BC/EC, black carbon/elemental carbon; PM, particulate matter.

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 $PM_{2.5}$-unadjusted model

We chose at random 15 studies included in the meta-analysis. Then, we extracted analysis items (outcomes, predictors, covariates, and lags) and calculated the search spaces. Table 2 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 analysis search spaces for the 15 studies chosen from the meta-analysis

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

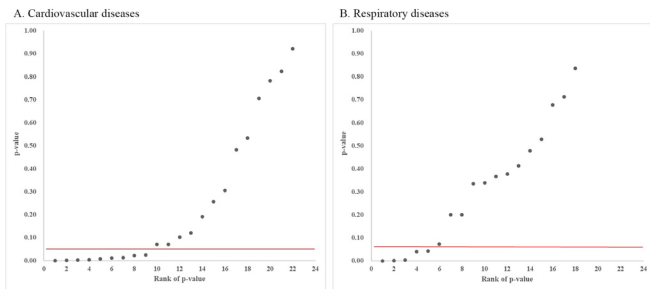

Figure 3 P value plots of short-term exposure to BC/EC on cardiovascular diseases (A) and respiratory diseases (B) in the $PM_{2.5}$-unadjusted model. BC/EC, black carbon/elemental carbon; PM, particulate matter.

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 $PM_{2.5}$-adjusted model, six studies were included in the meta-analysis of short-term exposure to BC/EC and cardiovascular diseases (RR 1.014 per 1 μg/m^3, 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 $PM_{2.5}$-unadjusted model. In addition, the impact of BC/EC on cardiovascular morbidity in the $PM_{2.5}$-adjusted model (RR 1.018 per 1 μg/m^3, 95% CI 1.006 to 1.031) was consistent with the results in the $PM_{2.5}$-unadjusted model (RR 1.022 per 1 μg/m^3, 95% CI 1.016 to 1.029). However, an increased risk was found between BC/EC and cardiovascular mortality in the $PM_{2.5}$-unadjusted model (RR 1.003 per 1 μg/m^3, 95% CI 1.001 to 1.006), while no association was observed in the $PM_{2.5}$-adjusted model (RR 1.006 per 1 μg/m^3, 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 μg/m^3, 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/m^3, 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 92]

The certainty of evidence on the acute effects of BC/EC on cardiovascular diseases in the $PM_{2.5}$-adjusted model was rated as 'moderate' and in the $PM_{2.5}$-unadjusted model was rated as 'low'. The evidence on the chronic effects of BC/EC on cardiovascular diseases was evaluated as 'moderate' certainty (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 $PM_{2.5}$-adjusted model and the $PM_{2.5}$-unadjusted model and sensitivity analysis showed that the associations were consistent. In contrast to the meta-analysis calculations, p value plots indicated mixed results for cardiovascular. Some studies indicated an effect while others appeared to be random. For respiratory effects, the p value plot was consistent with randomness, no effect. Our counting results, table 2 and 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 $PM_{2.5}$-adjusted model. Subgroup analysis indicated that the effects of BC/EC on cardiovascular diseases were the most significant on the current day and the impacts were decreased with lag days. In addition, the association between BC/EC and cardiovascular mortality in the cold season was stronger than that in the warm season. A potential reason could be that the concentration of BC/EC in the cold season was higher than that in the warm season.[97–99] Subgroup analysis on pollutant (BC and EC) indicated that the results from the $PM_{2.5}$-unadjusted model and $PM_{2.5}$-adjusted model were not consistent. Furthermore, the sensitivity analysis on omitting a single study showed that the results were not robust (data not shown). An essential reason could be that BC and EC were considered interchangeable. Three included studies simultaneously assessed the effects of BC/EC on cardiovascular diseases.[22 63 93] However, in the $PM_{2.5}$-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 $PM_{2.5}$-adjusted model and $PM_{2.5}$-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 $PM_{2.5}$.[102]

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 PM_{10} 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 short-term studies. Second, studies should adjust $PM_{2.5}$ when assessing the health effect of $PM_{2.5}$ constituents. Mostofsky *et al* showed that $PM_{2.5}$ may be associated with both health and its constituents. Constituents having closer association with $PM_{2.5}$ may illustrate a stronger association with diseases. Therefore, the results of $PM_{2.5}$-unadjusted model could introduce bias.[7] Third, further studies are suggested to evaluate the health effects of long-term exposure to BC, especially for morbidity. An essential difficulty that needs to be acknowledged is the availability of the disease data. Emergency department visits and outpatients are more time-sensitive data than mortality, hence these indicators are more representative to some extent in investigating the health effects of environmental factors. However, the data of emergency department visits and outpatients generally from medical institutions are more difficult to obtain than data on mortality, with a large portion of mortality data arriving from departments of disease control institutions in China. Forth, the present evidence on the health effects of BC was mainly from America and Asia. Studies assessing the association in other geographical locations are suggested, which might contribute to the evaluation of the potentially different effects of BC in different continents. Fifth, more studies need to provide evidence to prove the association between BC/EC and respiratory diseases in vulnerable populations.

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.

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SUPPLEMENTARY APPENDIX

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

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Supplementary data

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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 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.
#19	generalized additive model/or generalised additive model/or generalized linear model/or generalised linear model/or distributed lag non-linear model/or distributed lag nonlinear 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 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.

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	Diseases
Atkinson et al. 2016	TS	UK	2011-2012	Mortality	All	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Bell et al. 2014	TS	USA	2000-2004	Morbidity	≥65	BC	ICD-9	RES[COPD(ICD-9-CM:490–492,RTI(ICD-9-CM:464–466, 480–487)];CVD[HF(ICD-9-CM:428),Heart Rhythm Disturbances(ICD-9-CM:426–427), Cerebrovascular 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	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Hua et al. 2014	TS	China	2007-2012	Morbidity	0-14	BC	ICD-10	Asthma(ICD-10:J45)
Ostro et al. 2015a	CS	Spain, Greece	2008-2009 (Athens), 2009-2010(Barcelona)	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Samoli et al. 2016	TS	UK	2011-2012	Morbidity	≥15(CVD), all (RES)	BC,EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zanobetti and Schwartz 2006	CS	USA	1995-1999	Morbidity	≥65	BC	ICD-9	MI(ICD-9:410),Pneumonia (ICD-9: 480–487)
Liu et al. 2016a	TS	USA	2008-2013	Morbidity	All	EC	ICD-9	CVD(ICD-9:390-429),Stroke(ICD-9:430-438),RES(ICD-9:460-519),COPD(ICD-9:490-492,494,496),Pneumonia(ICD-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 (ICD-9:480-486),Asthma(ICD-9:493)
Sarnat et al. 2015	TS	USA	2001-2003	Morbidity	All	EC	ICD9	CVD[IHD(ICD9:410–414),Cardiac Dysrhythmias(ICD9:427),CHF(ICD9:428),Other CVD (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 Design	Country	Study Period	Outcome	Age	Pollutant	ICD 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:I00-I98),CVD(ICD-10:I00-I99)
Peng et al. 2009	TS	USA	2000-2006	Morbidity	≥65	EC	ICD-9	CVD[Cardiac Dysrhythmias(ICD-9:428),Heart Rhythm Disturbances(ICD-9:426-427),Cerebrovascular Events (ICD-9:430-438),IHD (ICD-9:410-414, 429),PVD(ICD-9:440-448)],RES[COPD(ICD-9:490-492),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)
Basagaña et al. 2015	CS	Spain, Italy	2003-2013	Morbidity, Mortality	All	EC	ICD-9, ICD-10	CVD(ICD-9:390-459,ICD-10:I00-I99),RES(ICD-9:460-519,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:I00-I99)
Cao et al. 2012	TS	China	2004-2008	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Klemm et al. 2011	TS	USA	1998-2007	Mortality	≥65	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99)
Zhou et al. 2011	TS	USA	2002-2004	Mortality	All	EC	ICD-10	CVD(ICD-10:I01-I99),RES(ICD-10:J00-J99)
Winquist et al. 2015	TS	USA	2001-2003	Morbidity	All	BC,EC	ICD-9	RES(ICD-9:460-465,466.0,466.1,466.11,466.19,477,480-486,491,492,493,496,786.07),CVD(ICD-9:410-414,427, 428,433-437,440,443-445,451-453)
Ostro et al. 2007	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J98)
Tolbert et al. 2000	TS	USA	1998-2000	Morbidity	All	EC	ICD-9	CVD(ICD-9:402,410-414,427,428,433-437,440,444,451-453),RES(ICD-9:460-466,477,480-486,491,492,493,496, 786.09)

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

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD 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:I60-I66)
Ostro et al. 2008	TS	USA	2000-2003	Mortality	All	EC	ICD-10	CVD(ICD-10:I00-I99)
Ito et al. 2011	TS	USA	2000-2006	Morbidity, Mortality	≥40	EC	ICD-9, ICD-10	CVD[Hypertensive Diseases(ICD-9:402,ICD-10:I11),MI(ICD-9:410;ICD-10:I21-I22),IHD (ICD-9:414,ICD-10:I25),Dysrhythmias(ICD-9:427,ICD-10:I48),HF(ICD-9:428,ICD-10:I50),Stroke(ICD-9:430-43 9,ICD-10:I60-I69)]
Chen et al. 2014	TS	China	2004-2008	Morbidity	All	EC	ICD-9	Stroke[Ischemic Stroke(ICD-9:433-434),Hemorrhagic Stroke(ICD-9:430-432)]
Tomic´-Spiric´ et al. 2019	CS	Serbia	2012-2014	Morbidity	≥18	BC	ICD-10	Allergic RES[AR(ICD-10:J.30.4),AA(ICD-10:J.45.0)]
Maynard et al. 2007	CS	USA	1995-1997, 1999-2002	Mortality	All	BC	ICD-9, ICD-10	CVD(ICD-9:390-429,ICD-10:I01-I52),Stroke(ICD-9:430-438,ICD-10:I60-I69),RES(ICD-9:460-519,ICD-10:J00-J 99)
Sinclair et al. 2010	TS	USA	1998-2002	Morbidity	All	EC	NR	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.

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	Diseases
Tolbert et al. 2007	TS	USA	1993-2004	Morbidity	All	EC	ICD-9	CVD[IHD(ICD-9:410-414),Cardiac Dysrhythmias(ICD-9:427),CHF(ICD-9:428),PVD and Cerebrovascular Events(ICD-9:433-437,440,443-445,451-453)], RES[Asthma(ICD-9:493,786.07,786.09),COPD(ICD-9:491,492,496),URTI(ICD-9:460-465,460.0,477),Pneumonia (ICD-9:480-486),Bronchiolitis(ICD-9:466.1,466.11,466.19)]
Lall et al. 2011	TS	USA	2001-2002	Morbidity	≥65	EC	ICD-9	RES[Pneumonia(ICD-9:480-486),COPD(ICD-9:490-492,496),Acute Bronchitis and Bronchiolitis(ICD-9:466),Asthma(ICD-9:493)],CVD[Dysrhythmia(ICD-9:427),IHD(ICD-9:410-414),HF(ICD-9:428),Stroke(ICD-9:431-437)]
Jung and Lin 2017	CS	China	2000-2010	Morbidity	0-20	BC	ICD-9	Asthma(ICD-9-CM:493)
Gong et al. 2019	TS	China	2006-2011	Mortality	All	BC	ICD-10	CVD(ICD-10:I00-I99)
Mostofsky et al. 2012	CS	USA	2003-2008	Morbidity	≥21	BC	NO	Acute Ischemic Stroke
Krall et al. 2017	TS	USA	1999-2009(Atlanta,Georgia), 2004-010(Birmingham,Alabama, 2001-2007(St.Louis, Missouri), 2006-2009(Dallas,Texas)	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 Wheeze(ICD-9:493,786.07)]
O'Lenick et al. 2017	CS	USA	2001-2008	Morbidity	5–18	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Pearce et al. 2015	TS	USA	1999-2008	Morbidity	5–17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.07)
Strickland et al. 2010	CS	USA	1993-2004	Morbidity	5-17	EC	ICD-9	Asthma(ICD-9:493.0-493.9),Wheeze(ICD-9:786.09),ARI(ICD-9:460.0-466.0)

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

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD 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, Mortality	all (mortality), ≥65(morbidity)	EC	ICD-9, ICD-10	CVD(ICD-10:I01-I79),RES(ICD-10:J00-J99)
Ostro et al. 2015b	Co	USA	2001-2007	Mortality	≥30	EC	ICD-10	CVD(ICD-10:I00-I99),IHD(ICD-10:I20-I25),Pulmonary(ICD-10:C34,J00-J98)
Gan et al. 2013	Co	Canada	1999-2002	Morbidity, Mortality	45-85	BC	ICD-9, ICD-10	COPD(ICD-9:490-492,496,ICD10:J40-J44)
Hvidtfeldt et al. 2019	Co	Denmark	1993-2015	Mortality	50 –64	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J99,C34)
Thurston et al. 2016	Co	USA	1988-2004	Mortality	≥30	EC	ICD-9, ICD-10	IHD(ICD-9:410-414,ICD-10:I20-I25)
Yang et al. 2018	Co	China	1998-2011	Mortality	≥65	BC	ICD-10	CVD(ICD-10:I00-I99),RES(ICD-10:J00-J47,J80-J99)
Gan et al. 2011	Co	Canada	1999-2002	Morbidity, Mortality	45–85	BC	ICD-9, ICD-10	CHD(ICD-9:410-414,429.2),(ICD-10:I20-I25)
De Kluizenaar et al. 2013	Co	Netherlands	1991-2003	Morbidity	15-74	EC	ICD-9	IHD(ICD-9:410-414),CHD(ICD-9:430-438)
Vedal et al. 2013	Co	USA	1994-2005	Morbidity, Mortality	50-79	EC	ICD-9	CVD (ICD-9:CM 410-452)
Rahmatinia et al. 2021	TS	Iran	2014-2017	Mortality	All	BC	ICD-10	RES(ICD10:J00- J99),CVD(ICD10:I00-I99),IHD(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	Co	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.

Study	Study Design	Country	Study Period	Outcome	Age	Pollutant	ICD code	Diseases
Wang et al. 2019b	CS	USA	2005-2016	Morbidity	All	BC	NR	STEMI
Ljungman et al. 2019	Co	Sweden	1990-2011	Morbidity, Mortality	All	BC	ICD-9, ICD-10	IHD(ICD-9:410–414 and ICD-10:I20-25);stroke(ICD-9:431–436 and ICD-10:I61– I65)
Liu et al. 2021a	Co	Sweden, Denmark	1992-2004	Morbidity	All	BC	ICD-9, ICD-10	COPD(ICD-9:490–492, and 494–496, or ICD-10:J40–44)

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; AA: allergic asthma; AR: allergic rhinitis; AMI: acute myocardial infarction; CA: cardiac arrest; STEMI: ST segment elevation myocardial infarction; RTI: respiratory tract infection; URTI: Upper Respiratory Infection; LRTI: Lower Respiratory Infection; ARTI: Acute respiratory infections.

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

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

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
Cardiovascular Diseases	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**
	11	Winquist,2015	1.048000	1.012000	1.085000	0.046884	0.011929	0.081580	0.017768	2.638621	**0.008324**
	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	lnRR	lnCI low	lnCI high	SE	Z	p-values
Respiratory Diseases	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**
	9	Heo,2014	0.988000	0.962000	1.015000	0.012073	0.038741	0.014889	0.013681	0.882435	**0.377541**
	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.

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

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

Risk of bias rating: Low | Probably Low | Probably High | High

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 et al. 2016	Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
		All of the pollutants were measured at the central London background monitoring site at North Kensington. All measurements were 24-h averages except for CO. The number of all observations was 621-693 (<25% missing data).	Death data for the period 1 January 2011 to 31 December 2012 were obtained from the Office for National Statistics. Daily counts of deaths in London, United Kingdom were classified as all disease-related causes, cardiovascular (International Classification of Diseases,10th revision-ICD10: I00-I99) and respiratory (ICD10: J00-J99) diseases.	Adjusted for time (seasonality, long-term trend), temperature, humidity, day of week and public holidays.	Study included daily counts of deaths in London, United Kingdom for the period 1 January 2011 to 31 December 2012.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare no conflict of interest.	No other potential sources of bias identified.

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

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

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 al. 2013	Single, central-site monitor. Daily BC and $PM_{2.5}$ were measured continuously and 24hr averaged was estimated if >75% of the 1hr values was available for that day. Missing data was not replaced by other values.	Health data were obtained from Shanghai Municipal Center of Disease Control and Prevention database. The causes of death were coded according to the International Classification of Diseases, Revision 10 (ICD 10).	Models included time (seasonality, long-term trend), temperature, humidity and day of week.	Data consisted of all causes (excluding accidents or injuries) deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare no conflict of interest.	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 High	Low	Probably Low	Low	Low	Probably Low	Low	Low
5	Hua et al. 2014	Daily 24h average $PM_{2.5}$ and BC data was obtained from a fixed-site station. The study only used the actual collected data and did not fill in the missing data for $PM_{2.5}$ and black carbon.	Daily asthma hospital admission data was obtained from Shanghai Children's Medical Center. Dates of admission and discharge, and diagnoses using the International Classification of Diseases, Revision 10.	Adjusted for long-term and seasonal trend, day of week, temperature and relative humidity.	Study included all asthma hospital admissions of children ≤ 14 years of age from Shanghai Children's Medical Center between1 January 2007 and 31 July 2012 in nine urban districts of Shanghai.	Daily counts for asthma hospital admissions of children were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

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: I00I99), respiratory (ICD9:460519, ICD10:J00J99) and all-cause mortality for those greater than age 65.	Adjusted for long term and seasonal (year, month, day of week) trends, temperature, holidays, summer vacations and influenza.	Study population consisted of daily counts of all-cause mortality for all ages and daily counts of cardiovascular, respiratory and all-cause mortality for those greater than age 65.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing interests.	No other potential sources of bias identified.

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 al. 2016	Daily concentrations of BC and EC were collected from the ClearfLo project, supplemented by local measurements made at the North Kensington urban background site. Number of days of observation for BC: 629 (BC urban in $PM_{2.5}$) and 702 (BC in $PM_{2.5}$) between 2011 and 2012 (<25% missing data).	Based on the primary discharge diagnosis, daily numbers of admissions for cardiovascular disease (International Classification of Diseases, 10th revision-ICD-10: I00-I99) for those aged 15-64 (adult) and 65+ years (elderly), and respiratory diseases (ICD-10: J00-J99) for those aged 0-14 years (paediatric), adult and the elderly were calculated.	Adjusted for long term and seasonal trends, temperature, relative humidity, regulated pollutants (PM_{10}, $PM_{2.5}$, NO_2, SO_2 and O_3), day of the week and public holidays.	Study included all cardiovascular and respiratory hospital admissions in London, UK between 2011 and 2012.	Daily counts for all emergency hospital admissions were obtained, so likely have all outcome data. However, any potential errors or missing data did not 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**
		Probably High	Low	Probably Low	Low	Low	Probably Low	Low	Low
8	Zanobetti and Schwartz 2006	Ambient BC from one monitor. The hourly measurements for BC and $PM_{2.5}$ were not complete. Missing values were replaced with the predicted values. Additionally BC data was missing from March 1997 to March 1999 and was not included in the study.	The study extracted data on all hospital admissions for residents of the Boston Metropolitan area who were admitted to the hospital (in the Boston area) with a primary diagnosis of MI (International Classification of Diseases, 9th revision-ICD-9:410), and pneumonia (ICD-9: 480–487), from Medicare billing records for the years 1995–1999.	Adjusted for temperature, day of the week, seasonality, long-term trends, humidity, barometric pressure, and the extinction coefficient.	Data consisted of all U.S. Medicare hospital admissions in the Boston Metropolitan area for myocardial infarction during the study duration.	Daily counts for hospital admissions were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing interests.	No other potential sources of bias identified.

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

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	24hr average concentration of $PM_{2.5}$ were obtained from a Supersite (single, central site monitoring location). The observations of EC was 666 days during 1 June 2001-30 April 2003 (missing data <25%).	Computerized billing records were obtained from the Missouri Hospital Association (MHA) for emergency department visits. The outcome groups were identified using primary International Classification of Diseases 9th Revision (ICD9) codes.	Models adjusted for season, day of week, holidays, time trends (using cubic splines for day of visit with monthly knots), and temperature.	Data consisted of all emergency department visits during the study period for cardiovascular disease outcomes.	Daily counts for emergency department visits were obtained, hence one hospital not providing data after 26 April 2002. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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

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

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. 2015	Daily 24-hour composite $PM_{2.5}$ samples were collected from single, central-site monitor. The observations of EC was 1809 days from 2003 through 2007 (missing data <25%).	Daily mortality counts for metropolitan Denver were computed from the Colorado Health Information Dataset compiled by the Colorado Department of Public Health and Environment. Data included cause of death by the International Classification of Diseases 10th Revision (ICD-10) code.	Models adjusted for longer-term temporal trend, as time since the study began, day of week, and daily temperature and humidity.	Data consisted of all deaths over the course of the study in a defined geographical area.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	None of the authors has any actual or potential competing interests.	No other potential sources of bias identified.

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
		Probably Low	Low	Probably Low	Probably Low	Low	Probably Low	Low	Low
15	Huang et al. 2012	Daily average concentrations of $PM_{2.5}$ were obtained from a single, central-site monitor. Daily average concentrations of EC in $PM_{2.5}$ samples were further analyzed. Daily data was available and no missing data was reported.	Daily mortality data were obtained from the Xi'an Center for Disease Control and Prevention. The International Classification of Diseases, Tenth Revision (ICD-10), codes of mortality were as follows: all natural causes (ICD-10 codes A00–R99), respiratory diseases (ICD-10 codes I00–I98), and cardiovascular diseases (ICD-10 codes I00–I99).	Models adjusted for calendar time (seasonality, long-term trends), weather(temperature, relative humidity), year, day of week.	The author removed the death counts on December 31 and January 1 of each year.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

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

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. 2012	The U.S. Environmental Protection Agency established the PM Speciation Trends Network (STN) to measure more than 50 $PM_{2.5}$ chemical components, in addition to total mass. The STN includes > 50 national air monitoring stations (NAMS) and > 200 state and local air monitoring stations (SLAMS). Air pollution concentrations were typically measured on a 1-in-3-day schedule in the NAMS and on a 1-in-6-day schedule in the SLAMS. There was no information about missing data.	Hospital admissions data were obtained from billing claims information for US Medicare enrollees in 119 counties for the years 2000–2008. The Medicare billing claims data were classified into disease categories according to their International Classification of Diseases, Ninth Revision (ICD-9), codes.	Adjusted for time (seasonality, long-term trends), seasonality, day of the week and dew-point temperature.	Study included people who died any day between 2000 and 2008 in 119 US counties.	Daily counts of hospital admissions were obtained from billing claims information, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

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

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

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

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

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. 2016a	The concentrations of different particle size fractions and $PM_{2.5}$ chemical constituents were measured at two air monitoring stations. EC were measured for four months of each year from 2007 through 2010. During the period 2009-2011, the proportion of missing data was very low (ranging from 1% to 2%). There were about 20 days without chemical constituents records and were treated as missing observations.	Daily mortality data from 1 January 2007 to 31 December 2011 were obtained from Guangdong Provincial Center for Disease Control and Prevention. The cause of death was coded using the International Classification of Diseases, Tenth Revision (ICD-10). Mortality from cardiovascular diseases (ICD-10:I00-I99) were extracted to construct the time series.	Adjusted for public holidays, day of the week, influenza outbreaks, seasonal patterns and long-term trends, temperature and relative humidity.	Study included daily cardiovascular mortality data from 1 January 2007 to 31 December 2011 in Guangzhou.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial 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**
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
23	Cao et al. 2012	Daily concentrations of EC was obtained from a single monitoring site. The observations of EC was 1749 in 1827 days (missing data <25%).	The study obtained numbers of deaths in Xi'an for each day from the Shanxi Provincial Center for Disease Control and Prevention (SPCDCP). SPCDCP staff then classify the cause of death according to the International Classification of Diseases, 10th Revision [ICD-10; World Health Organization (WHO) 1992] as due to total nonaccidental causes (ICD-10 codes A00–R99), cardiovascular diseases (I00–I99), respiratory diseases(J00–J98), or injury (S00–T98).	Model adjusted for long-term and seasonal trends, day of week, temperature, humidity, and SO_2 and NO_2 concentrations.	Data consisted of all nonaccidental causes deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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

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. 2011	24hr $PM_{2.5}$ samples were obtained from a single, central-site monitor. Daily data was available and no missing data was reported.	Using codes from the International Classification of Diseases, version 10 (ICD10; World Health Organization 2007), daily death counts were aggregated to nonaccidental allcause deaths (ICD10, codes A00 through R99), cardiovascular deaths (ICD10, codes I01 through I99), and respiratory deaths (ICD10, codes J00 through J99).	Models adjusted for time, seasonality and long-term trends, day of week, temperature, and humidity.	Data consisted of all cardiovascular deaths over the course of the study.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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

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

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

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

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 al. 2014	Daily 24-hour average EC was from ambient monitoring networks. Missing data <1%.	Health data were obtained from 41 metropolitan Atlanta hospitals and the Georgia Hospital Association. The diagnoses of respiratory infection were based on International Classification of Diseases, 9th Revision (ICD-9), diagnosis codes: acute bronchitis or bronchiolitis (code 466); pneumonia (codes 480–486); and upper respiratory infection (codes 460–465).	Adjusted for dew point, temperature, seasonality, long-term trends, day of week, holiday and influenza epidemics.	Study included daily emergency department visit data from 41 metropolitan Atlanta hospitals for the period January 1, 1993, to December 31, 2004 (not all hospitals contributed the full period), and from the Georgia Hospital Association for the period January 1, 2005, to June 30, 2010.	Daily counts for emergency department visit were obtained. In the earliest years of the study, not all hospitals were participating. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

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

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 cause of death as identified by the International Classification of Diseases, Ninth Revision (ICD-9, World Health Organization, Geneva).	Adjusted for time trend, seasonality, day of week, temperature and relative humidity.	Data consisted of all cardiovascular deaths during over the course of the study.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

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

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

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. 2016b	Each of the six counties had two monitors measuring components of $PM_{2.5}$. Fresno, Kern, Riverside and Sacramento counties reported 24-hour average EC in $PM_{2.5}$ every third day; San Diego and Santa Clara counties reported data every sixth day. The study included only species for which at least 50% of the observations were above the level of detection.	Daily mortality for all California residents were obtained from the California Department of Health Services, Center for Health Statistics. Daily counts of deaths from cardiovascular disease (International Classification of Diseases, Tenth Revision (ICD10) =I00–I99) were calculated.	Adjusted for time, temperature, humidity and day of the week.	Study included daily cardiovascular mortality for all California residents from 1 January 2000 to 31 December 2003.	Daily counts for death were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that 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
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
36	Ito et al. 2011	Ambient EC obtained from multiple monitors and the average of data from multiple monitors was computed using the 24hr average values. The sampling frequency of the chemical speciation data was every third day. Daily data was available and no missing data was reported.	Hospitalizations and mortality data were available at the New York City Department of Health and Mental Hygiene. The relevant variables available in the electronic discharge abstract for each patient included date of admission and International Classification of Diseases, Nine Revision (ICD9) discharge diagnosis code. The International Classification of Diseases, Tenth Revision (ICD10) codes for determining cause of death.	Model adjusted for temporal trends and seasonal cycles, immediate and delayed temperature effects, and day of the week.	Data consisted of all cardiovascular hospital admissions over the course of the study.	Daily counts for death and hospitalization were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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

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´-Spiric´ et al. 2019	Average daily concentrations of BC in micrograms per cubic meter were measured by three automatic ambient air quality monitoring stations. There was no information about missing data.	Emergency department visits data were obtained from the Health Center Užice, either from the emergency department visits in Užice, Sevojno, and Kosjeri´ c, or from a general hospital in Užice. The inclusion criteria were adults aged 18 years and older with the diagnosis of allergic rhinitis (International Classification of Diseases, 10th revision, code J.30.4), allergic asthma (International Classification of Diseases, 10th revision, code J.45.0), or asthma with coexisting allergic rhinitis.	Adjusted for temperature, humidity, and air pressure.	Study included emergency department visit for allergic rhinitis and allergic asthma from 1 July 2012 to 30 June 2014 in the Zlatibor District, Western Serbia.	All counts for emergency department visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial interests.	No other potential sources of bias identified.

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 et al. 2007	Daily measurements of BC were obtained from a single monitor site. In order to predict local BC level, the study used a validated spatial–temporal land use regression model to predict 24-hr measures of traffic exposure data (BC) at > 80 locations in the Boston area.	Individual mortality records were obtained from the Massachusetts Department of Public Health, for the years 1995–2002. Specific cause mortality was derived from the International Classification of Diseases (ICD) codes [9th Revision before 1999 (World Health Organization 1975) and 10th Revision 1999 to 2002 World Health Organization 1993)].	Adjusted for season and long term trend, temperature, dew point and day of week.	Study included all death for all causes, cardiovascular, respirator, stroke, and diabetes diseases in Boston metropolitan area from the Massachusetts Department of Public Health between 1995–1997 and 1999–2002.	Daily counts for individual mortality records were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no competing financial 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
		Probably Low	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
40	Sinclair et al. 2010	Daily 24-hr averages EC was from a single monitor site. The total observed rate of EC was 95.2%.	Daily outpatient visits were obtained from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002. Visits that met acute visit definition and that had a visit diagnosis code of asthma, upper respiratory infection (URI), or lower respiratory infection (LRI) were included in the study.	Adjusted for season, day of week, federal holidays, study month, time, temperature and dew point.	Study included daily outpatient visits for acute respiratory diseases from the electronic patient data warehouse of a not-for-profit, group-model managed care organization (MCO) in the metropolitan Atlanta area between August 1, 1998 and December 31, 2002.	Daily counts for outpatient visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

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

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

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

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

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

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 al. 2019	The 24-h mean BC concentrations data were obtained from a single monitor site. During the study period (2091 days), missing rate of BC was 0.68%.	The disease data used in this study were collected from the Chinese Center for Disease Control and Prevention, and included all deaths in Beijing from January 1, 2006 to December 31, 2011. Causes of death were classified according to the International Classification of Diseases, 10th Edition (ICD-10) and data on cardiovascular diseases (ICD-10 code: I00–I99) were obtained.	Adjusted for calendar effects, long-term trends, temperature, humidity, day of week, NO_2 and SO_2.	Study included all cardiovascular mortality in Beijing obtained from the Chinese Center for Disease Control and Prevention during January 1, 2006 to December 31, 2011.	Daily counts for all deaths were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Authors declared no conflict of interest.	No other potential sources of bias identified.

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

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. 2017	$PM_{2.5}$ constituents from one urban, ambient monitor located in each city. Daily pollution data were available in Atlanta; however, data were only available approximately every third day in the remaining three cities. There was no information about missing data.	The study obtained electronic billing data for respiratory disease emergency department visits for all ages at acute care hospitals. Using diagnosis codes from the International Classification of Diseases, 9th Revision (ICD-9), the study considered subcategories of respiratory diseases including pneumonia (ICD-9 codes 480–486), chronic obstructive pulmonary disease (491,492,496), upper respiratory infection (URI) (460–465, 466.0, 477), and asthma and/or wheeze (493, 786.07).	Adjusted for holidays, long-term trends, day of the week, season, hospitalsreporting data, temperature and dew point.	Study included all emergency department visits for respiratory disease at acute care hospitals in the 20-county Atlanta metropolitan area, the 7-county Birmingham metropolitan area, the 8 Missouri and 8 Illinois counties in the St. Louis metropolitan area, and the 12-county Dallas metropolitan area.	Daily counts for emergency department visits of respiratory disease were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial 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
		Probably Low	Low	Probably Low	Low	Low	Probably Low	Low	Low
49	O'Lenick et al. 2017	The 24-hour average concentration of EC was evaluated. Pollutant concentration estimates were obtained by fusing observational data from available network monitors with pollutant concentration simulations from the Community Multi-Scale Air Quality emissions-based chemical transport model at 12×12km grids over Atlanta. 24-hour average EC were evaluated. Daily data was available and no missing data was reported.	Patient-level emergency department visit data from 1 January 2002 to 31 December 2008 were acquired from hospitals located within the 20-county metropolitan area of Atlanta; Relevant data elements included admission date, International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes, age and ZIP code of patient residence.	Adjusted for season, periods of hospital participation and holidays, temperature and mean dew point, interaction terms between season and maximum temperature and day of year.	Study included all emergency department visit data acquired directly from hospitals (2002–2004 period) and the Georgia Hospital Association (2005–2008 period) located within the 20-county metropolitan area of Atlanta.	Daily counts for emergency department visit were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	Competing interests: None declared.	No other potential sources of bias identified.

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

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

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

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

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 al. 2015b	The model calculations track the mass and concentrations of the PM constituents in particle diameters ranging from 0.01 to 10μm through calculations that describe emissions, transport, diffusion, deposition, coagulation, gas- and particle-phase chemistry, and gas-to-particle conversion. The University of California Davis/California Institute of Technology model was used to estimate ground-level concentrations of 50 PM constituents over the major population regions in California.	Deaths were assigned codes based on the International Classification of Diseases, 10th Revision (ICD-10) for the following outcomes: all-cause deaths excluding those with an external cause (A00–R99), cardiovascular deaths (I00–I99), Ischemic heart disease deaths (I20–I25), and pulmonary deaths (C34, J00–J98).	ge, race, marital status, smoking status, pack-years of smoking, secondhand smoke exposure, body mass index, lifetime physical activity, alcohol consumption, average daily dietary intake of fat, calories, menopausal status, family history of myocardial infarction, stroke, use of blood pressure medication, aspirin; living conditions	Data obtained for a cohort of female teachers ≥30 years old.	There was no 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 they have no actual or potential competing financial 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
				(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. 2013	Using high spatial resolution land use regression models to estimate residential exposure to traffic-related air pollutants including black carbon. During the 5-year exposure period, individual exposures to ambient air pollutants were estimated at each person's residential postal code centroid using land use regression models.	The study used International Statistical Classification of Diseases, 9th Revision (ICD-9) codes 490–492 and 496 or 10th Revision (ICD-10) codes J40–J44 to identify COPD cases during the 4-year follow-up period.	Individual-level covariates: age, sex, preexisting comorbid conditions; and neighborhood socioeconomic status (SES).	Data obtained for a cohort of people (45-85 years old) registered with the provincial health insurance plan. Study provided total number of subjects along with those lost during the follow-up period.	During the 4-year follow-up period, 38,377 (8%) subjects were lost to follow-up because of moving out of the province or dying from other diseases.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial 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
		Probably Low	Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
56	Hvidtfeldt et al. 2019	The PM, NO_2, BC, and O_3 concentrations at residential addresses of the cohort members were derived by a high-resolution dispersion modelling system which incorporates contributions from local, urban, and regional sources of precursors to PM, NO_2, BC, and O_3.	Participants who died from external causes such as injuries, accidents and suicides (International Classification of Diseases, 10th Revision-ICD-10 codes S–Z) were censored at date of death. In addition, the study investigated cardiovascular (ICD10 codes I00–I99) and respiratory (ICD10 codes J00–J99 and C34) subgroups of mortality.	Age, sex, educational attainment, occupational status, marital status, smoking (status, intensity, and duration), environmental tobacco smoke (ETS), alcohol consumption, body mass index, waist circumference, fruit consumption, vegetable consumption, physical activity; neighborhood level socioeconomic status (SES).	Data obtained for a cohort of men and women aged 50–64 years residing in the areas of Copenhagen and Aarhus.	There was no 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 they have no competing financial 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
		Probably Low	Probably Low	Probably High	Low	Probably High	Probably Low	Low	Low
57	Thurston et al. 2016	The mean concentrations of $PM_{2.5}$ mass and trace constituents were obtained from U.S. Environmental Protection Agency Air Quality System. These $PM_{2.5}$ constituent data were analyzed to derive estimates of source apportioned $PM_{2.5}$ mass exposure concentrations using the absolute principal component analysis (APCA) $PM_{2.5}$ source apportionment method.	More than 99% of known deaths were assigned a cause using the International Classification of Diseases, 9th and 10th Revision (ICD-9 codes 410–414; ICD-10 codes I20–I25).	Active smoking and former smoking, passive smoke exposure, possible workplace exposure to PM, occupational dirtiness index, marital status, education, BMI and BMI^2, consumption of beer, wine, and other alcohol, quintile of dietary fat consumption, quintile of combined dietary vegetable, fruit, fiber consumption; Six ecologic covariates.	Data obtained for a cohort of persons at least 30 years of age, in households including someone at least 45 years of age and resided in all 50 states, the District of Columbia, and Puerto Rico.	The analytic cohort included 445,860 participants, with 34,408 Ischemic heart disease deaths (of a total of 157,572 deaths from all causes) occurring during follow-up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No competing financial interests.	No other potential sources of bias identified.

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

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. 2011	Land use regression to estimate air pollution concentrations and exposure assigned to residential centroid.	A coronary heart disease hospitalization case is a record of hospitalization with the following International Statistical Classification of Diseases, 9th Revision codes, ICD-9, 410–414 and 429.2or 10th Revision (ICD-10), I20–I25, as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the hospitalization database. A coronary heart disease death is a death record with coronary heart disease as the cause of death in the provincial death registration database.	Model adjusted for age, sex, preexisting comorbidity, and neighborhood socioeconomic status. No individual data on behavioral risk factors.	Study provided total number of subjects along with those lost during the follow-up period.	During the 4-year follow-up period, 17,542 (3.9%) moved out of the province and 16,367 (3.6%) died from other diseases, leaving 418,826 (92.5%) subjects at the end of follow-up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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 Kluizenaar et al. 2013	Used black smoke (BS) as an indicator of EC concentrations. Derived background EC concentrations from BS measured at two regional monitoring sites. Local traffic-related EC emission contributions were estimated based on fuel-specific EC content of exhaust PM_{10} emission. Used the traffic-related EC emissions as input to calculate local EC concentrations, assuming absence of other local EC sources. Also assumed that dispersion dynamics of EC are identical to those of PM_{10}.	The study obtained information on the incidence of hospital-based Ischemic heart disease (International Classification of Diseases [ICD9] 410-414) and cerebrovascular disease (ICD9 430-438) in the study population.	Individual-level covariates: age, gender, marital status, education, smoking, alcohol use, physical activity, body mass index, living conditions (employment status, financial problems).	Data obtained for a cohort of 27,070 non-institutionalized subjects.	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.	No competing financial 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
		Probably Low	Probably Low	Probably Low	Low	Probably Low	Probably Low	Low	Low
61	Vedal et al. 2013	The exposure estimation were used the national spatial model predictions and secondary exposure measures of citywide average exposures and distance to major roadways.	All outcomes were reported via questionnaire and assessed via physician-adjudicator review of medical records following established protocols.	Individual-level covariates: age, body mass index, smoking status, cigarettes smoked per day and years of smoking, systolic blood pressure, history of hypertension, hypercholesterolemia, history of diabetes, education, household income level, and race.	Data obtained for a cohort of postmenopausal women.	There was no information on the rate of lost follow up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	No financial interests.	No other potential sources of bias identified.

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

No.	Study	Exposure assessment	Outcome assessment	Confounding bias	Selection bias	Incomplete outcome data	Selective reporting	Conflict of interest	Other
63	Liu et al. 2021b	Probably Low	Probably Low	Probably Low	Low	Low	Probably Low	Low	Low
		Annual county-level exposures of PM2.5 and its constituents for each participant were assessed by aggregating satellite-derived estimates at a monthly time-scale and 1 km-resolution.	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-demography 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 relationships 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 al. 2021	A spatial PM2.5 surface gridded at a resolution of approximately 1-km2 was derived using multiple satellite-based retrievals of aerosol optical depth in combination with a chemical transport model, and enhanced through statistical incorporation of ground- based observations (including BC).	Incident childhood asthma cases were identified according to International Classification of Diseases [ICD]-10: J45.	Model adjusted for parity, child sex, breastfeeding status at the time of discharge, maternal smoking during pregnancy, maternal atopy, gestational age and birth weight.	The study used data on singleton live births that occurred between April 1st 2006 and March 31st 2014 in the Province of Ontario, Canada. Mother-infant pair data were obtained from the Better Outcomes Registry & Network (BORN) Ontario, a province wide birth registry that captures perinatal health information.	There was no information on the rate of lost follow up.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declared that there is no conflict of interest.	No other potential sources of bias identified.

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
65	Rodins et al. 2020	The study used the validated, time-dependent, three-dimensional European Air Pollution Dispersion chemistry transport model (EURAD) to estimate the exposure to EC.	Cardiovascular outcomes in the HNR Study were determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records.	Model adjusted for age, sex, individual and neighborhood SES, BMI, nighttime traffic noise exposure and lifestyle factors: smoking, alcohol consumption, physical activity and nutritional pattern.	The study used baseline (2000–2003) and 14 years follow-up data from the German HNR Study, an ongoing population-based prospective cohort study.	There was no 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 relationships 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	Low	Probably Low	Low	Low
66	Kovačević et al. 2020	The daily average concentration of BC were collected from three automatic ambient air quality monitoring stations located in Užice, Sevojno, and Kosjerić. BC were measured between 1st July 2012 and 30th June 2014. There was no information about missing data.	The data of emergency department (ED) visits for allergic asthma were collected from the Užice Health Centre, either from the EDs (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice. International Classification of Diseases, 10th revision, codes were used in the diagnosis of allergic asthma or asthma with coexisting allergic rhinitis (AR).	Model adjusted for seasonality, long-term trends, temperature, humidity, air pressure, air pollutants and pollens.	Study included all the data of emergency department (ED) visits for allergic asthma were collected from the Užice Health Centre, either from the EDs (ambulances or home care) in Užice, Sevojno, and Kosjerić or from a general hospital in Užice during 1st July 2012 to 30th June 2014.	Daily counts for emergency department (ED) visits were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare no conflict of interest.	No other potential sources of bias identified.

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 al. 2020	BC levels were modelled using EnviMan (Opsis AB, Sweden) by the Environmental Department of Malm¨o. The program uses a Gaussian dispersion model (AERMOD) combined with an emission database for the county of Scania in Sweden.	The outcomes were plaque presence and CIMT of the right carotid artery, which were assessed by ultrasound examination B-mode ultrasonography, conducted by trained and certified sonographers.	Model adjusted for age, sex, air pollutant, education level, smoke score, apoB/apoA1 ratio, use of lipid lowering drugs, living alone, cardiovascular heredity, diabetes mellitus, waist hip ratio, physical activity, alcohol consumption, median income level in residential area, systolic blood pressure and being born outside of Sweden.	In the cardiovascular subcohort of the MDCS cohort, 6031 participants who had a residential address within the air pollution modelling area. Of these, 224 were missing data on plaque and 20 on CIMT, respectively. The number of participants included in the plaque analyses were 5807 and in the CIMT analyses 6011.	Of these, 224 were missing data on plaque and 20 on CIMT, respectively. Hence, the number of participants included in the plaque analyses were 5807 and in the CIMT analyses 6011.	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 High	Probably Low	Probably High	Low	Low	Probably Low	Low	Low
68	Wang et al. 2019b	BC were collected from a routine air quality monitoring site operated by the New York State Department of Environmental Conservation continuously throughout the study period (2005–2016). There was no information about missing data.	All patients treated at the Cardiac Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY for STEMI, who resided within 15 miles of the pollution monitoring station in Rochester were included. American College of Cardiology (ACC)/American Heart Association (AHA) guidelines were used at the time of Cath Lab admission to diagnose STEMI.	Model adjusted for seasonality, long-term trends, temperature and relative humidity.	Study included all patients treated at the Cardiac Catheterization Laboratory (Cath Lab) at URMC in Rochester, NY for STEMI throughout the study period (2005–2016).	Daily counts for all patients were obtained, so likely have all outcome data. However, any potential errors or missing data did not depend on air pollution levels.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare that they have no competing interests.	No other potential sources of bias identified.

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 et al. 2019	Based on detailed emission databases, monitoring data, and high-resolution dispersion models, the study calculated source contributions to black carbon (BC) from road wear, traffic exhaust, residential heating, and other sources in Gothenburg, Stockholm, and Umeå.	The International Classification of Diseases, Ninth Revision (ICD-9) codes 410–414 and ICD-10 I20-25 codes were used to define IHD and ICD-9 codes 431–436 and ICD-10 codes I61– I65 were used to define stroke.	Model adjusted for sex, calendar year, subcohort, smoking 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 Market Statistics.	The study included individuals in two cohorts from Gothenburg, four pooled cohorts from Stockholm, and one cohort from Umeå. In total, 114,758 individuals were included from all study areas.	The study used high-quality and comprehensive national patient and death registries, minimizing loss to follow-up for our outcomes of interest. Missing information for variables ⩽ 5% not specified.	There was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report.	The authors declare they have no actual or potential competing financial interests.	No other potential sources of bias identified.

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. 2021a	Annual mean concentrations of BC for 2010 were estimated at the study participants' baseline residential addresses, using standardized Europe-wide hybrid land use regression (LUR) models. The LUR model utilized routine monitoring data from the European Environment Agency (EEA) AirBase for PM2.5, NO2, and O3, and ESCAPE monitoring data for BC as the dependent variable. BC was measured by the reflectance of PM2.5 filters and expressed in absorbance units.	COPD was defined by following the principal diagnosis of International Classification of Diseases, 9th Revision (ICD-9) codes 490–492, and 494–496, or ICD-10 codes J40–44.	Model adjusted for age, sex, smoking status, smoking duration, smoking intensity, body-mass index, marital status, employment status, educational level and area-level annual year income.	The study used data from three cohorts within the ELAPSE project with available information on COPD hospital discharge diagnoses. Mean follow-up time is 16.6 years.	From a total of 106,727 participants with complete air pollution exposure data, the study excluded 633 participants with COPD at baseline and 7,586 participants with missing information on confounders.	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 relationships that could have appeared to influence the work reported in this paper.	No other potential sources of bias identified.

Table S8 Assessment of certainty of evidence for the outcomes.

Evidence	Reasons for downgrading										Reasons for upgrading						Overall	Final certainty assessment
	A1	Rationale	A2	Rationale	A3	Rationale	A4	Rationale	A5	Rationale	B1	Rationale	B2	Rationale	B3	Rationale		
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.

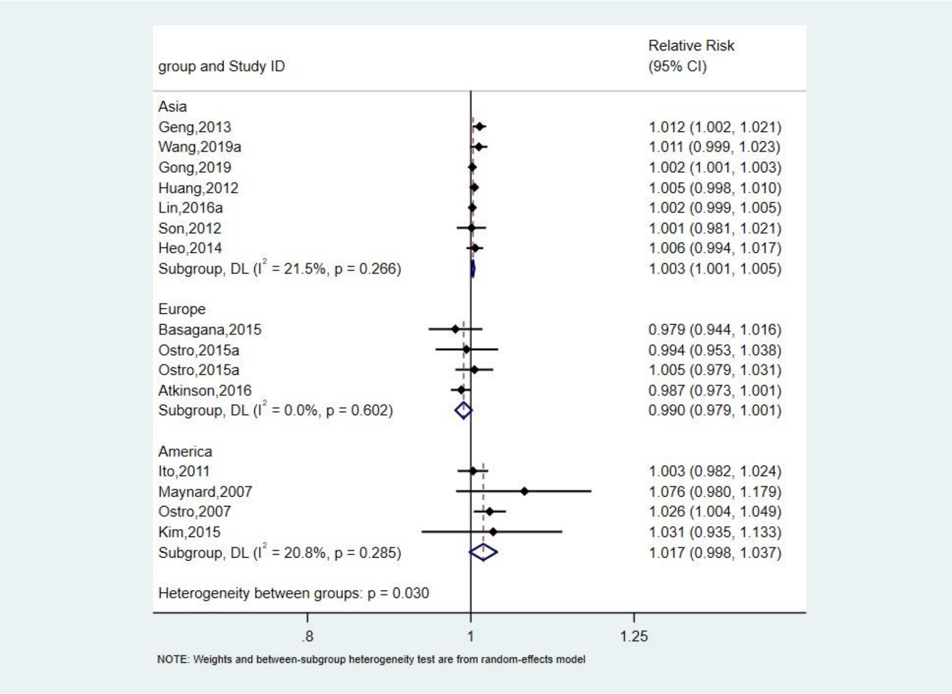

Figure S1 Impact of short-term exposure to BC/EC on cardiovascular mortality stratified by geographical locations.

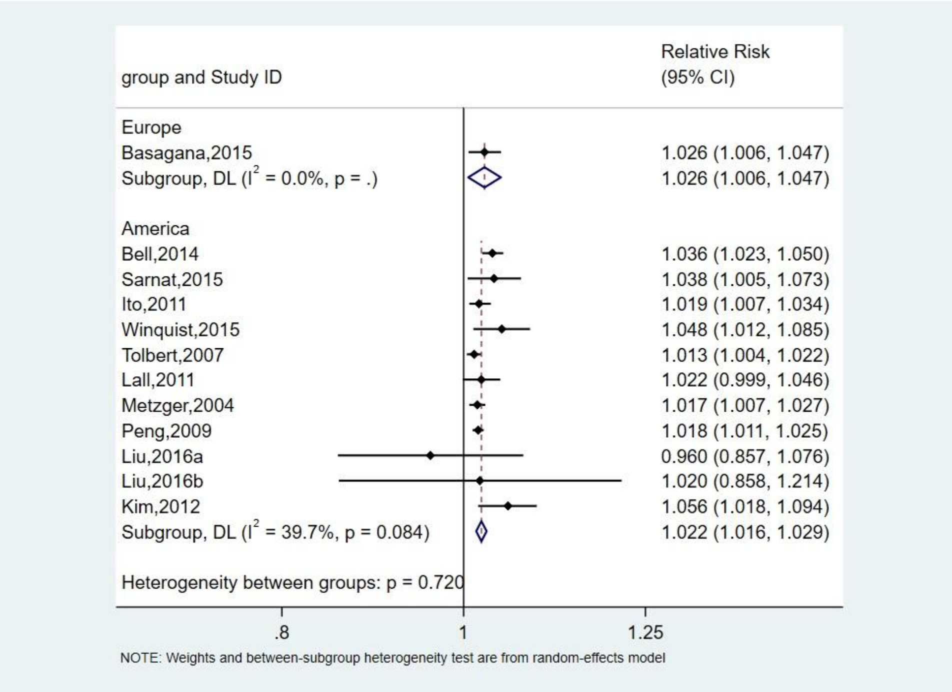

Figure S2 Impact of short-term exposure to BC/EC on cardiovascular morbidity stratified by geographical locations.

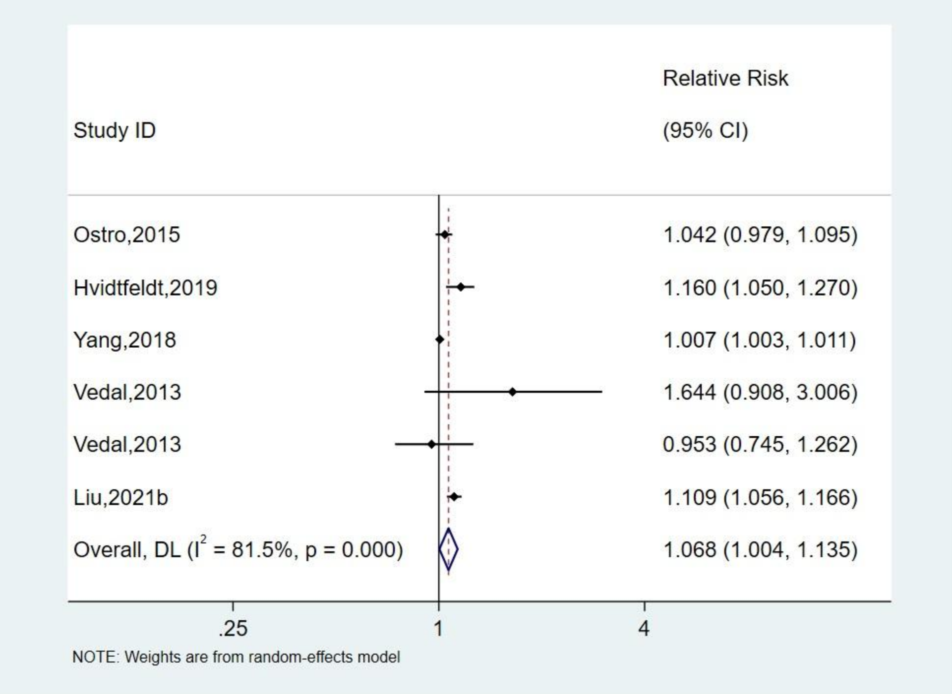

Figure S3 Impact of long-term exposure to BC/EC on cardiovascular diseases.

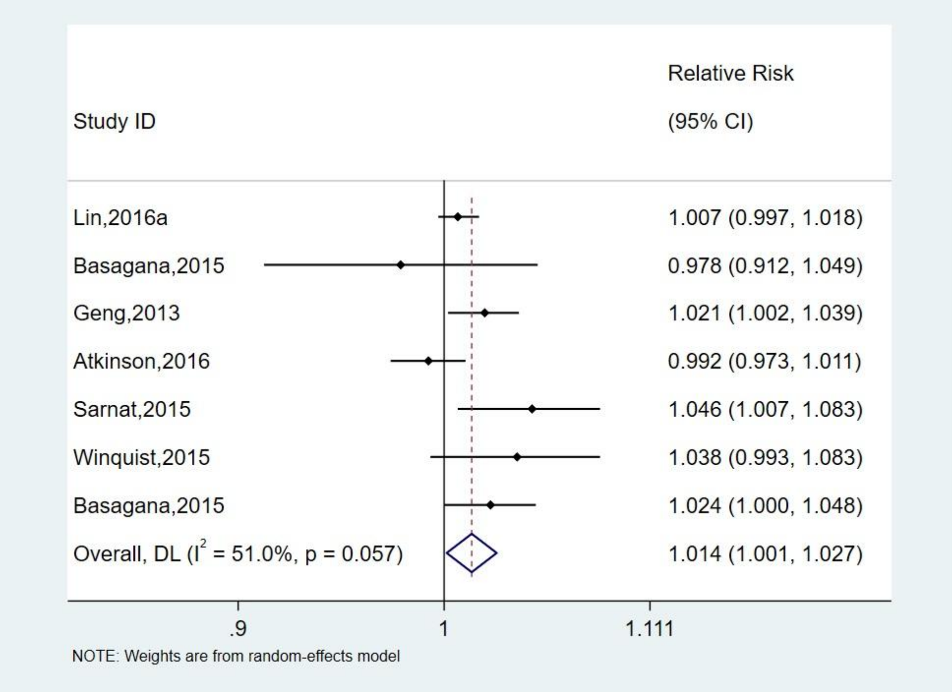

Figure S4 Impact of short-term exposure to BC/EC on cardiovascular diseases in the $PM_{2.5}$-adjusted model.