BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031312
Article Type:	Research
Date Submitted by the Author:	01-May-2019
Complete List of Authors:	sun, zhuanlan; Tongji University, Zhu, Demi; Shanghai Jiaotong University
Keywords:	outdoor air pollution, health outcomes, evidence gap map

Exposure to outdoor air pollution and its human-related health outcomes: an evidence gap map

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ABSTRACT

Objectives Outdoor air pollution is a serious environmental problem worldwide. However, the specific topic of systematic review findings on particular factors cannot be used to provide a comprehensive overview of air pollution related health outcomes. This study aimed to comprehensively identify gaps in current evidences and inform future research priorities.

Methods Four electronic databases, PubMed, Cochrane, Scopus, and Web of Science, were searched from their inception until June 2018. Citations and reference list of included studies were also traced so that more relevant studies were gathered. The inclusion and exclusion criteria were used to screen the titles and abstracts of studies by two reviewers independently. Characteristics of the included studies were extracted and summarized. Bubble plot was used to visually display outdoor air pollution, health outcomes, literature size, and a broad strength of findings.

Design Evidence gap map.

Results Of the 86 inclusive systematic review and meta-analysis studies, most of them had been conducted in Europe, Asia and North America. Most of the studies (27/86; 31%) included primary studies that had been conducted between 5 to 10 countries. The largest population affected by outdoor air pollution fell under the group of all ages (46/86; 53%), the group of children and adolescents under the age of 20 affected by outdoor air pollution accounted for a proportion of 17%, and the smallest population fell under the group of infants and elderly. The bubble plot showed that most studies reported the health outcomes of cardiovascular diseases, respiratory diseases, and health records, which were mainly affected by fine particulate matter or mixed air pollution.

Conclusions This evidence gap map provided a visual overview of health outcomes affected by outdoor air pollution exposure and some evidence gaps were identified. Research agendas were lacking on health outcomes of chronic diseases, cancer and mental disorders.

Strengths and limitations of this study

This evidence gap map provides an overview of a broad range of systematic review and meta-analysis studies based on four databases from their inception until June 2018.

This visualized evidence gap map focused on health outcomes affected by outdoor air pollution, it supported the evidence-based information for environmental policymaking and identified evidence gaps for potential research prioritization.

Only English-language SRs, thus possibly missing pertinent information written in other languages.

INTRODUCTION

Outdoor air pollution, a serious environmental problem and major concern of public health worldwide, has linked to approximately 4.2 million global deaths in 2016 [1]. It is a severe invisible killer of human health particularly in developing countries where the industrialization and urbanization developed quickly [2]. There are many common and prevalent types of air pollutants, such as fine particulate matter ($PM_{2.5}$, PM_{10}), ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_2 and NO_x), volatile organic pollutants and some other toxic air pollutants, the topic of human-related health outcomes affected by such air pollutants have been studied for decades. Researchers from various disciplines all over the world have shown constant interest in health effects of outdoor air pollution, such as cardiovascular disease, respiratory disease, cancer, Alzheimer's disease and so on [3–6].

Systematic reviews (SRs) aim to synthesis all relevant quality assessed evidence on a specific topic in terms of the health outcomes of outdoor air pollution [7].It was reported that outdoor NO_2 exposure triggered asthma [8 9], other studies identified human mortality was positively associated with $PM_{2.5}$ exposure [10 11]. However, many studies focused on interactive effects with regard to several types of health outcomes affected by various air pollutants [12 13], and there are some overlapping SRs conducted on the same topic implied inconsistent results [14 15]. The specific topic

of SRs findings on particular factors cannot be used to provide a comprehensive overview of air pollution related health outcomes.

To overcome this barrier, some novel knowledge synthesis approaches (e.g., scoping review, systematic mapping, evidence mapping etc.) have been developed to evaluate the overall effect of evidence on a broader area, highlighting both what is known and gaps in evidence [16–19]. Evidence gap map (EGM), an emerging synthesis method, was proposed to systematically and comprehensively assess intervention effects and outcomes in a user-friendly two-dimensional matrix framework. It can also visualize the existing evidence in a map with critical quality appraisal for policy and research implications [20 21].

EGM can inform a strategic approach to build the evidence based on particular issues. Water, sanitation and hygiene interventions were evaluated by 3ie to inform policy decision and address evidence gap [21]. To our knowledge, there are few researches use EGM to visually present the evidence across a broader topic on outdoor air pollution exposure related health outcome topics. We constructed an EGM on the health effects of outdoor air pollution to gather relevant evidence by using visual approaches. Our research will comprehensively collected as much extensive evidences as possible from existing SRs and meta-analyses. The main purpose of this EGM was to support the evidence-based information for environmental policymaking and to identify the evidence gaps for potential research prioritization.

MATERIALS & METHODS

EGM is an newly developed knowledge synthesis methods based on evidence mapping, since no standard methodology was available for evidence mapping [22]. We followed the methodology framework presented by Snilstveit et al to construct this EGM. The framework was divided into six steps: developing scope; setting inclusive criteria; searching relevant studies; selecting studies; extracting data and appraising quality; and summarizing results.

Scope development

The established framework was two-dimensional matrix of outdoor air pollution and health outcomes, it derived from the major policies of interest and existing academic literatures. The row and column of the framework included all categories of outdoor air pollution and human-related health outcomes respectively. A consultation with key stakeholders, including academic researchers, policymakers, practitioners and funders were involved to make sure the acceptance of the framework.

Study inclusion criteria

We followed 3ie's guideline to include systematic review and meta-analysis studies and to synthesize all the available evidence on human-related health outcomes affected by particular air pollution [23].

Study search

Four electronic databases, PubMed, Cochrane, Scopus, and Web of Science, were searched from their inception until June 2018. The language was restricted to English. We compiled a list of outdoor air pollution and health outcome terms by reviewing the potential text words in the titles or abstracts of the most pertinent literatures (supplemental table s1), this process was conducted by consulting with experts who are members of the Committee on Public Health and Urban Environment Management in China. We then used advanced database search strategies on key words, combined with Boolean operators (AND, OR, NOT) and wild card symbols (*), so as to search for the potentially relevant literatures (supplemental table s2). To prevent any relevant literatures from missing, we subsequently traced citations and reference list of included literatures to generate more relevant systematic review and meta-analysis studies.

Inclusion assessment

The first step of inclusion evaluation involved screening the titles and abstracts of studies by two reviewers independently. The inclusion and exclusion criteria for evidence gap map were discussed by the team members at the beginning of this process (table 1). Reference management software Mendeley was used to systematically remove duplicated literatures and assess potential literatures that meet the inclusion criteria.

Table 1 Inclusion and exclusion criteria used in this EGM for eligible studies

Inclusive criteria	Exclusive criteria
Studies types	**Studies type**
SRs or meta-analyses	Indoor air pollution
Studies methods	
Quantitative reviews or combined with qualitative reviews	**Studies methods**
Studies conclusion	Qualitative reviews only
Data supported outcome relevant to outdoor air pollution	

The second step of the study selection stage was the full text retrieve of all potentially eligible articles, which was independently screened by the two reviewers as well. If disagreements occurred between them, a third specialist made the final decision.

Data extraction and critical appraisal

Characteristics of the included studies were extracted and summarized by one reviewer and checked for accuracy by the other. Extracted data included authors, publication year, continent, discipline, study design, study duration, sample size, study region, target population, types of air pollution, and health outcomes (table 2). Other categories, such as key results, will extract based on the interest of policymakers.

The potential study designs and the inherent characteristics (strengths and limitations) of each design make the quality assessment complex [24]. We applied the Supporting the Use for Research Evidence (SURE) checklist [21] to appraise the quality of included SRs and meta-analyses in terms of the confidence, rating them as high, medium or low confidence [20]. We assessed the quality of included studied by using SURE checklist rather than AMSTAR, GRADE and ROBBINS,

because SURE was a mechanism aims to strengthen the evidence-informed policymaking, which is more appropriate for our study purpose.

Table 2 Information to be collected during the data extraction stage

Study design	Study population	Exposures	Outcome information
Author(s)	Sample size	Air pollution	Health outcomes
Publication Year	Study region		Key results
Discipline	Target population		
Continent			
Study design			
Study duration			

Summarization and visualization

To provide a snapshot of what it is known and where evidence is lacking, a bubble plot was used to represent extend of health outcomes affected by outdoor air pollution. We followed the visual representation of 3ie's two-dimensional framework [21] to generate the bubble plot. Traffic light color in the plot indicated the confidence of findings in the SRs and meta-analysis studies based on the SURE checklist, bubbles size represented the quantity of corresponding studies.

Patient and public involvement

No patient or public involved in this evidence gap map.

RESULTS

Figure 1 displayed the systematic literatures search process for evidence gap map. Literature search of four electronic databases yielded 361 potentially relevant studies. Of the 266 unique studies, 118 SRs and meta-analyses were assessed as being relevant based on screening the titles and the abstracts. To avoid missing potential studies, we searched the relevant studies on the top five impact factor periodicals in our database, downloading citations and reference lists of these relevant studies and assessing them by using the inclusion criteria, then 5 more relevant studies were included at the end of this process. In total, 123 systematic review and meta-analysis studies were included in the full-text screening analysis and the finial 86 eligible articles were included in our EGM.

General descriptions summary of included studies

Of the included 86 studies, most of them were conducted in Europe, Asia and North America, with the proportion of 37%, 34% and 22% respectively (table 3). As illustrated in figure 2, the systematic review and meta-analysis studies conducted in the top three continent were concentrated in a small group of countries, with China, USA, and UK on the top of the list. Little evidences came from Africa, Australia, and South America, with an overall proportion of only 6%.

The population of included studies ware categorized into seven subgroups: infants, children and adolescents, adults, women and pregnancy, all ages, elderly, and not specified (table 3). The largest population affected by outdoor air pollution fell under the group of all ages (46/86; 53%),

followed by the group of children and adolescents under the age of 20, with the percentage of 17% (15/86). Health outcomes in the groups of adults and women and pregnancy accounted for the proportion of 8% and 5% respectively, infants and elderly groups shared the same proportion of only 2%.

The population of included studies came from more than one country. Most of the studies (27/86; 31%) included primary studies that had been conducted in 5 to 10 countries, 21% of the studies had been conducted in less than 5 countries, and 17% of those had been conducted in the countries that numbered between 10 to 20. The samples size of the primary study in the inclusive studies varied with a wide range, the number of which ranged from less than one hundred to millions (range: 83-11,850,884 participants).

Table 3 General descriptions for included studies

(n=86)	N	%		N	%
Continent [a]			**Numbers of original study**		
Africa	1	1%	<10 studies	10	12%
Australia	2	2%	10~30 studies	46	53%
South America	3	3%	30~60 studies	13	15%
North America	19	22%	>60 studies	13	15%
Asia	29	34%	Not clearly mentioned	4	5%
Europe	32	37%	**Study period**		
Countries included in inclusive studies			<10 years	11	13%
<5 countries	18	21%	10 ~ 20 years	23	27%
5 ~ 10 countries	27	31%	> 20 years	7	8%
10 ~ 20 countries	15	17%	Not clearly mentioned	45	52%
> 20 countries	1	1%	**Types of study design**		
Not clearly mentioned [b]	25	29%	Single	13	15%
Population			Multiply	73	85%
Infants	2	2%	**Study design**		
Children & Adolescents	15	17%	Cohort	41	
Adults	7	8%	Case-crossover	27	
elderly	2	2%	Time-series	25	
Women & Pregnancy	4	5%	Case-control	24	
All ages	46	53%	Cross-sectional	20	
Not specified	10	12%	**Sample size(range)**	(83-11,850,884)	

Of the study design, 15% (13/86) of the included studies were conducted by using single study design, the rest 73 studies originated from primary studies with multiply study designs. The top five mostly popular study designs used in the primary studies of inclusive studies were cohort, case-crossover, time-series, case-control, and cross-sectional, the corresponding number were 41, 27, 25, 24, and 20 respectively.

Summary of inclusive studies in six research fields

The included SRs and meta-analyses were mainly conducted in six research fields. As the cumulative frequency trend chart displayed in figure 3, the number of the studies showed an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years, with no studies published before the year 2004. There was an increasing trend in the

number of publications in the fields of medicine and public environmental occupational health from 2004 to 2013, and the trend remarkably raised from 2013 till now, especially in medicine researches. The environmental sciences saw a rising trend since 2011, then the trend spiked up in the years of 2012 and 2015 respectively, and reached its peak number in 2017. Three disciplines, including environmental sciences and public environmental occupational health, multidisciplinary, and neurosciences, increased smoothly since the year 2011.

Summary by health outcome groups

We categorized health outcomes into eight groups based on the specialists' suggestions: cardiovascular diseases, chronic diseases, health records, cancer, mental disorders, respiratory diseases, pregnancy and children, and other diseases, which are important features of the EGM visualization. The categorized list of health outcomes were showed in table 4.

Table 4 The categorized list of health outcomes

Health outcome groups [a]	Health outcome of inclusive studies
Respiratory diseases	Asthma, respiratory diseases, ALRI
Chronic diseases	Diabetes
Cardiovascular diseases	Hypertension, BP, COPD,OHCA,VTE,CVD, myocardial infarction, Arrhythmia , stroke
Health records	Morbidity, hospital admissions, ED visits, mortality
Cancer	Lung cancer
Pregnancy & Children	Fertility, pregnancy, Birth
Mental disorders	Mental health, cognition, ASD
Other diseases	Physical inactivity, skin disease, health risks

[a]: ALRI: acute lower respiratory infections, BP :blood pressure ,COPD: chronic obstructive pulmonary disease, OHCA: out-of-hospital cardiac arrest, VTE: venous thrombo embolism, CVD: cardiovascular diseases, ED: emergency department, ASD: autism spectrum disorder.

The inclusive studies in our database were summarized based on health outcome groups (table 5). The information of the types of air pollution, number of original study, population group, sample size, and key finding were included in the table 5. Of the 86 identified SRs and meta-analyses, 24 studies reported cardiovascular diseases as outdoor air pollution related health outcomes, the figures of health records and respiratory diseases studies that had been reported as an adverse effect of outdoor air pollution exposure were 22 and 19 respectively. Each of the rest five groups of health outcomes accounted for an average studies of 4. All SRs and meta-analyses included more than 10 primary studies at least, health outcomes in all ages account for the largest groups in all categories, expect for those of respiratory diseases category, in which children was the most suffered ones.

Overall, mixed air pollution was the dominant type of outdoor air pollution, which tended to show a positive harmful effect in all health outcome groups. What's more, it was the main cause of the respiratory diseases among children and the chronic diseases among people in all ages.

EGMs visualization

The feature of EGMs is to provide a visual display of evidence from the systematic reviews. Bubble plot was used to display the types of air pollution and related health outcomes in a two dimensional matrix framework, as presented in figure 4. The colors of bubble in the map represent the confidence of SRs and meta-analyses, which is assessed by SURE checklist [25]. Red color of bubble represents low confidence and yellow color of bubble means medium confidence. The sizes of bubble indicate the relative number of included studies, a larger bubble represents a larger study sample size in each grid. Confidence result of identified studies were showed in supplemental table s3.

Table 5 Characteristics of included studies based on health outcome groups

Health outcome group (number of studies)	Types of air pollution [a] (number of studies)	Number of original study (mean +/- STD)	Population group (number of studies)	Sample size (range)	Key finding
Cardiovascular diseases (24)	Fine particulate matter (10) General air pollution gas (1) Mixed air pollution (13)	32 +/- 30	Infant & children (1) Adults & old (5) All ages (16) Other (2)	（83, 11,850,884）	Positive (22) Ambiguous (2)
Chronic diseases (2)	Mixed air pollution (2)	11 +/- 2	All ages (2)	（402, 62,012）	Positive (2)
Health records (22)	Fine particulate matter (10) General air pollution gas (4) Other toxic substances (1) Mixed air pollution (7)	40 +/- 38	Infant & children (1) Adults & old (1) All ages (15) Other (5)	（1,050, 50,756,699）	Positive (21) Negative (1)
Cancer (4)	Fine particulate matter (1) Mixed air pollution (3)	24 +/- 10	Adult (1) All ages (3)	（29, 500,000）	Positive (4)
Mental Disorders (5)	General air pollution gas (1) Other toxic substances (1) Mixed air pollution (3)	16 +/- 10	Infant & children (2) All ages (2) Other (1)	（252, 7,203）	Positive (3) Negative (1) Ambiguous (1)
Respiratory diseases(19)	Fine particulate matter (3) Other toxic substances (1) Mixed air pollution (15)	37 +/- 31	Infant & children (11) Adults & old (1) All ages (6) Other (1)	（186, 1,146,215）	Positive (18) Negative (1)
Pregnancy & children (6)	Fine particulate matter (2) Mixed air pollution (4)	23 +/- 22	Infant & children(1) All ages(3) Other(2)	（263, 3,545,177）	Positive (6)
Other diseases (4)	Fine particulate matter (2) Other toxic substances (1) Mixed air pollution (1)	35 +/- 48	Adults & old (1) All ages(2) Other(1)	（73, 2,381,292）	Positive (3) Negative (1)

a : Mixed means the combination of general air pollution gas and fine particulate matter, toxic substances not include.

Most studies reported the health outcomes of cardiovascular diseases, respiratory diseases, and health records, which were mainly affected by fine particulate matter or mixed air pollution. Little studies investigated other toxic substances and its adverse effect on human-related health outcomes. By identifying the evidence gaps that existed in the outdoor air pollution related health outcomes, more potential research agenda need to focus on chronic diseases, cancer and mental disorders, so that research gaps can be filled and evidence-based information can be provided to support precise policy-making. By highlighting the confidence of the existing evidence based on inclusive studies, policymakers can promote relevant policies based on the existing synthesized

evidences in outdoor air pollution related health outcomes. In addition, more high-quality SRs and primary studies and synthesized evidence across a range of disciplines were needed to ensure the confidence of existing evidence for the policy decision making.

DISCUSSION

This EGM provided the most up-to-date SRs by using the user-friendly visualization of the existing evidence in a matrix format of interventions and outcomes framework, so that it helps to set potential research agenda and promote evidence-based policy makings. EGM is novel evidence synthesized method in that they offer a reliable means of covering a broad scope of a particular sector, focusing on visualizing quality of the existing evidence in a user-friendly format. Most importantly, EGM can address evidence gaps for funding research with limited resources and provide evidence-based information to support precise policy-making.

This EGM is to collect and category a variety body of high-quality evidence to overview the health outcomes affected by outdoor air pollution. It includes 86 published SRs and meta-analyses. The visualized categories of outdoor air pollution and health outcomes reveals the research gaps and concentrations of the existing literatures. The diseases mostly affected by outdoor air pollution concentrate on cardiovascular diseases, respiratory diseases and health records, including COPD, BP, hypertension, asthma, morbidity, and mortality. The major air pollution types are fine particulate matter ($PM_{2.5}$, PM_{10}) and general air pollution gas (CO, SO_2, NO_2, and O_3), few health outcome studies was caused by other toxic air pollutants. Well-designed primary studies and meta-analyses on chronic diseases, cancer, especially metal disorders will needed in future research.

A major gap observed is lack of uniform diagnostic criteria of diseases. Criteria and reporting of air pollution related health outcomes were notably variable, with significant potential for subject heterogeneity. Future researches should define and report the diagnostic criteria more precisely. What's more, there is a difficulty in estimating the personal exposure of air pollution. The inconsistent exposure levels may probably lead the "exposure bias". Although the number of studies using the measurement of exposure time has increased, there is still room to use more precise estimation. In addition, the study period was not clearly reported. As we all know, even in the same country or region, industrialization and modernization made air pollution different between different time periods. These SRs should be updated. "Population bias" gap was also found in our EGMs. When including more children, for example, it could have overestimated the true prevalence of the disease. Clearly stratified analysis of different age groups is needed for the reason that outdoor air pollution has different impacts on different age groups.

Some important areas of air pollution research are left blank. For example, few of the SRs included healthcare costs related to outdoor air pollution. As the public focus on environmental sustainability become even stronger in recent years, the demand for studies may increase. Moreover, they should come as a warning to policymakers as it shows that actual evidence for the

healthcare costs related to outdoor air pollution. More precisely, studies aimed at economic burden of outdoor air pollution are needed.

Most SRs and meta-analyses in the included studies estimated the health outcomes affected by outdoor air pollution in general population rather than those with established disease, thus, summarization of the existing body of evidence should therefore be viewed in more researches that aim at evaluate the health outcomes of established disease affected by outdoor air pollution. Besides, researches focus on the physiological effects, such as increased heart rate and feelings of anxiety, are indispensable so that EGM can capture a comprehensive overview of air pollution related health outcomes. Geographically, it is worth noting that most of the available primary studies included in SRs were conducted in Western countries, where the median $PM_{2.5}$ concentration is less than 20 μg/m^3. In developing countries, however, the $PM_{2.5}$ concentrations in urban cities are likely to be up to 100μg/m^3. There is room for more robust impact evaluation by using subgroup analysis.

Limitations

Our EGM built on the evidence base from significant numbers of systematic reviews that have quantitatively addressed the health outcomes influenced by air pollution. The "gold standard" restriction on included studies may neglect important information available from studies. Since the main purpose of our EGMs is to provide a resource for policymakers, only inclusion of SRs is sufficient to generate reliable conclusions for policymakers [20]. Hundreds of quality appraisal methods exist in the synthesis knowledge studies [26], the efficiency of these studies depend largely on the quality assessment result, we only applied SURE checklist instead of other quality assessment methods in that it is more suitable for EGMs. Two reviewers assessed separately to prevent any bias occurred.

We evaluated only English-language SRs, thus possibly missing pertinent information written in other languages. Other designed primary studies, such as observational study, time series study and causal inference study, were not included. In addition, this EGM largely relied on information provided by included SRs, there may have been undetected errors of data abstraction or synthesis in one or more of the systematic reviews. Finally, research gaps identified in this EGM do not necessarily equate to research needs. It should consider that the desirability, feasibility, and importance of the research gaps, highlighting the importance of stakeholder engagement in this process.

CONCLUSIONS

This evidence gap map provided a visual overview of health outcomes affected by outdoor air pollution. Despite the outlined limitations, it is a useful tool to inform environmental policy decision makers. It also can promote further potential researches by visualizing and synthesizing high-quality systematic reviews and highlighting the absolute gaps. More prospective studies,

with large numbers of participants, are needed in developing countries. It will helpful to assess the long-term effects of air pollution more precisely.

Contributorship statement Zhuanlan Sun formulated the research question. Demi Zhu and Zhuanlan Sun devised the search strategy, consulting with experts from Committee on Public Health and Urban Environment Management in China. Demi Zhu and Zhuanlan Sun conducted the search, screened all titles, abstracts and full articles and extracted data. Demi Zhu and Zhuanlan Sun co-wrote the manuscript.

Competing interests None declared.

Funding This work was supported by a major projects of the National Social Science Fund of China grant number 13&ZD176.

Data sharing statement All data relevant to the evidence gap map are included in the manuscript.

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FIGURE LEGEND

Figure 1 Systematic literatures search process for eligible studies.

Figure 2 Regions and countries distribution of eligible studies.

The data of regions and countries are based on the information of corresponding authors.

Figure 3 Numbers of inclusive studies in six research fields between 2004 and 2018.

The number of the studies saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years.

Figure 4 Evidence gap map for health outcomes affected by outdoor air pollution. The colors of bubble represent the confidence of included studies, red color represents low confidence and yellow color represents medium confidence. The sizes of bubble indicate the relative number of included studies, and a larger bubble represents a larger study sample size in each grid.

TABLE LEGEND

Table 1 Inclusion and exclusion criteria used in this EGM for eligible studies.

Table 2 Information to be collected during the data extraction stage.

Table 3 General descriptions for included studies.

Table 4 The categorized list of health outcomes.

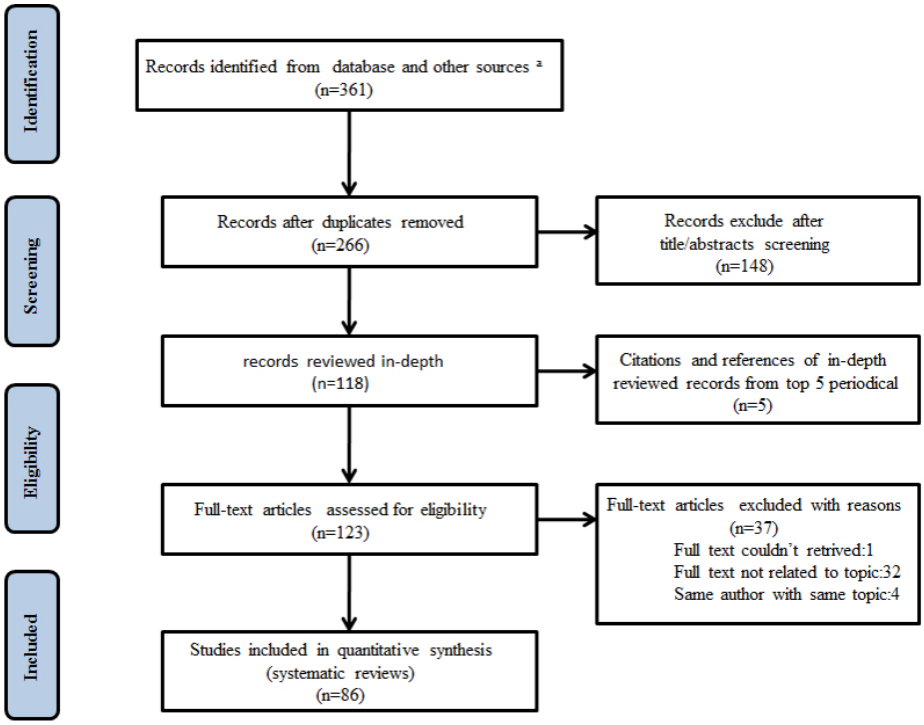
Table 5 Characteristics of included studies based on health outcome groups.

Supplemental Table S1 List of outdoor air pollution and health outcome related terms.

Supplemental Table S2 Search strategies for the potentially relevant studies.

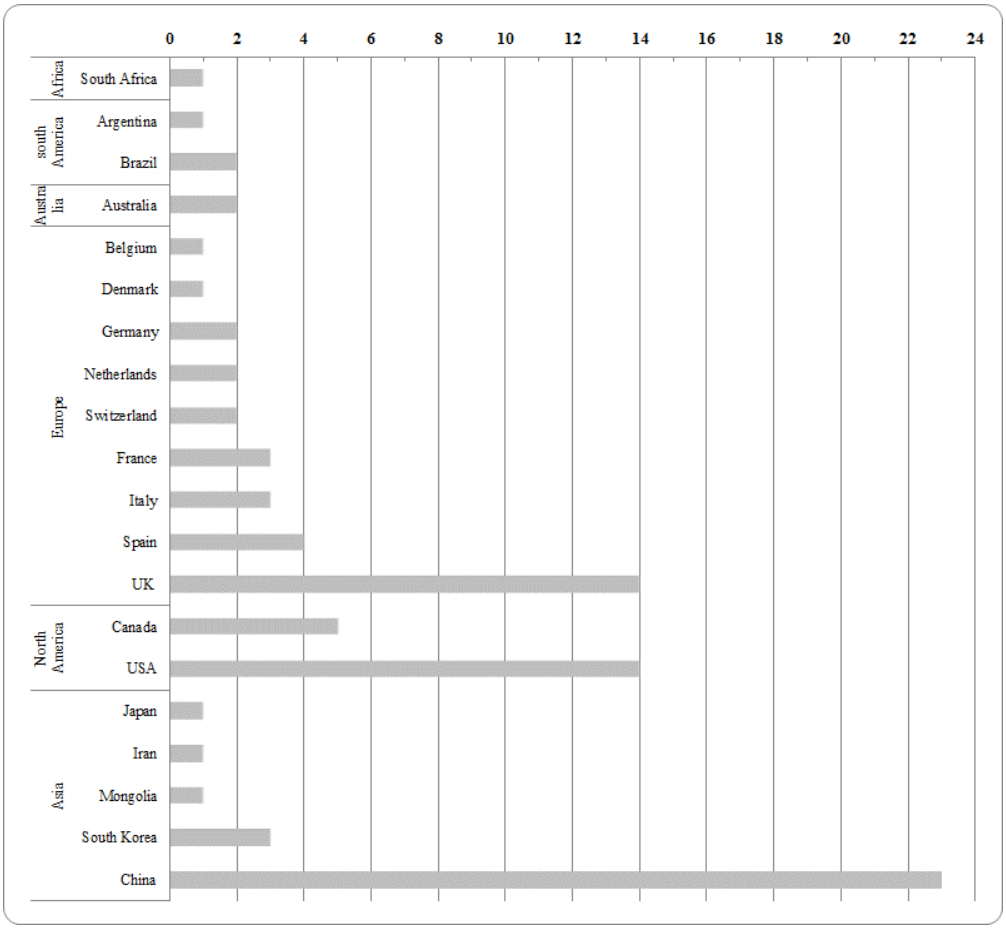
Supplemental Table S3 Confidence result of identified studies.

The list includes outdoor air pollution categories, health outcomes categories and the confidence result based on SURE.

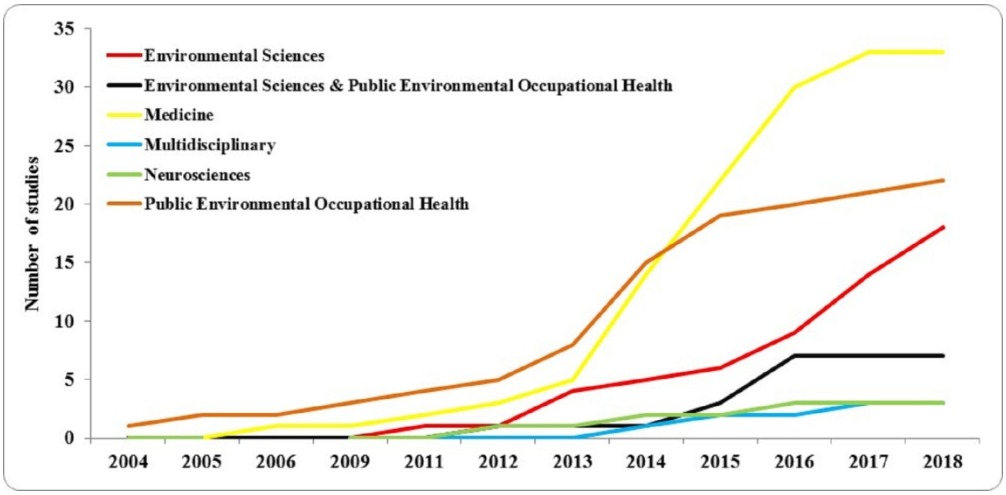


[a]: 59 form PubMed, 216 from Scopus and 86 from Web of Science

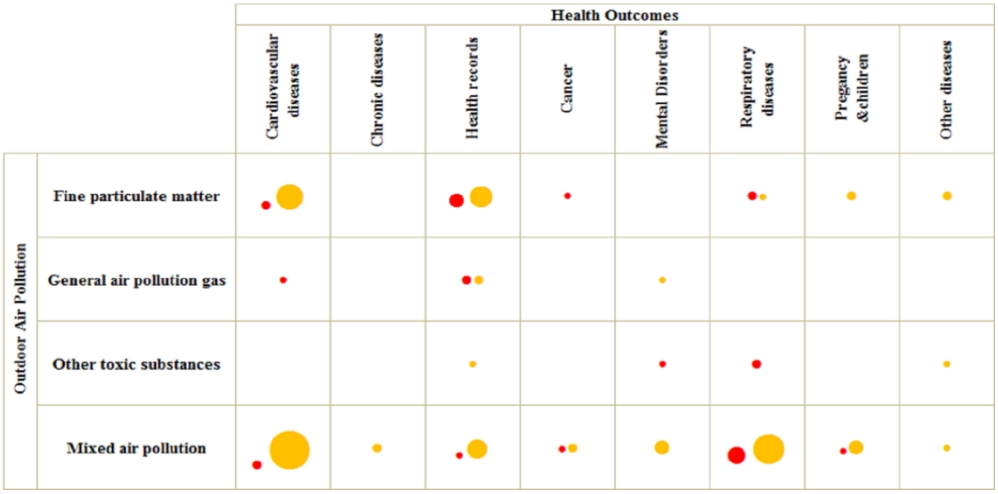
Systematic literatures search process for eligible studies.



Regions and countries distribution of eligible SRs and MAs. The data of regions and countries are based on the information of corresponding authors. SRs, systematic reviews; MAs, meta analyses.



Numbers of inclusive eligible SRs and MAs in six research fields between 2004 and 2018. The number of the eligible SRs and MAs saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years. SRs, systematic reviews; MAs, meta analyses.



Evidence gap map for health outcomes affected by outdoor air pollution.The colors of bubble represent the confidence of included studies, red color represents low confidence and yellow color represents medium confidence. The sizes of bubble indicate the relative number of included studies, and a larger bubble represents a larger study sample size in each grid.

Supplemental Table S1:

List of outdoor air pollution and health outcome related terms.

Concept	Type	Detail
Outdoor air pollution	General air pollution gas	ozone(O_3), sulfur dioxide(SO_2), carbon monoxide(CO), nitrogen dioxide(NO_2)
	Fine particulate matter	total suspended particle, suspended particulate matter,$PM_{2.5}$, PM_{10}
	Other toxic substances	toxic air pollutants, Volatile organic pollutants, nitrogen oxides (NO_x)
Health outcomes	Respiratory diseases	asthma, lung cancer, respiratory infections, respiratory disorder
	Chronic diseases	diabetes, chronic obstructive pulmonary disease
	Cardiovascular diseases	hypertension, heart rate variability, heart attack, cardiopulmonary disease, ischemic heart disease, blood coagulation, deep vein thrombosis, stroke
	Health records	morbidity, hospital admissions, outpatient visits, emergency room (ER) visits and mortality
	Other diseases	DNA methylation changes, neurobehavioral functions, inflammatory disease, skin disease, abortion, Alzheimer's disease, disability, cognitive function, Parkinson's disease

Supplemental Table S2 [a]:

Search strategies for the potentially relevant studies.

1. Database and time period

PubMed Clinical Queries Database – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	Search ((((((((((Ozone*[MeSH Terms]) OR sulfur dioxide*[MeSH Terms]) OR carbon monoxide*[MeSH Terms]) OR nitrogen dioxide*[MeSH Terms]) OR PM2.5[MeSH Terms]) OR PM10[MeSH Terms]) OR total suspended particle*[MeSH Terms]) OR suspended particulate matter*[MeSH Terms]) OR Toxic air pollutant*[MeSH Terms]) OR volatile organic pollutant*[MeSH Terms]) OR nitrogen oxide*[MeSH Terms]	138,175
#2	Search ((((((((((((((((((((((((((asthma[MeSH Terms]) OR lung cancer[MeSH Terms]) OR respiratory infection*[MeSH Terms]) OR respiratory disorder*[MeSH Terms]) OR diabetes[MeSH Terms]) OR chronic respiratory disease*[MeSH Terms]) OR chronic obstructive pulmonary disease*[MeSH Terms]) OR hypertension[MeSH Terms]) OR heart rate variability[MeSH Terms]) OR heart attack[MeSH Terms]) OR cardiopulmonary disease*[MeSH Terms]) OR ischemic heart disease*[MeSH Terms]) OR blood coagulation*[MeSH Terms]) OR deep vein thrombosis[MeSH Terms]) OR stroke[MeSH Terms]) OR morbidity[MeSH Terms]) OR hospital admission*[MeSH Terms]) OR outpatient visit*[MeSH Terms]) OR emergency room visit*[MeSH Terms]) OR mortality[MeSH Terms]) OR DNA methylation change*[MeSH Terms]) OR neurobehavioral function[MeSH Terms]) OR Inflammatory disease*[MeSH Terms]) OR skin disease*[MeSH Terms]) OR abortion[MeSH Terms]) OR Alzheimer's disease*[MeSH Terms]) OR	3,125,123

item	Search input	result
	disability[MeSH Terms]) OR cognitive function[MeSH Terms]) OR Parkinson's disease*[MeSH Terms]	
#3	Search (outdoor[Text Word]) AND air pollution[Text Word]	3,132
#4	meta analysis[Title/Abstract]	111,455
	#1 AND #2 AND #3 AND #4	0
	#3 AND #4	**44**
#5	systematic review[Title/Abstract]	111,428
	#1 AND #2 AND #3 AND #5	0
	#3 AND #5	**38**

After duplication: 59

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1. Database and time period

Scopus – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	TITLE-ABS-KEY ("Ozone*") OR TITLE-ABS-KEY ("sulfur dioxide*") OR TITLE-ABS-KEY ("carbon monoxide*") OR TITLE-ABS-KEY ("nitrogen dioxide*") OR TITLE-ABS-KEY (pm2.5) OR TITLE-ABS-KEY (pm10) OR TITLE-ABS-KEY (total AND suspended AND particle*) OR TITLE-ABS-KEY (suspended AND particulate AND matter*) OR TITLE-ABS-KEY (toxic AND air AND pollutant*) OR TITLE-ABS-KEY ("volatile organic pollutant*") OR TITLE-ABS-KEY ("nitrogen oxide*")	327,759
#2	TITLE-ABS-KEY ("asthma") OR TITLE-ABS-KEY ("lung cancer") OR TITLE-ABS-KEY ("respiratory infection*") OR TITLE-ABS-KEY ("respiratory disorder*") OR TITLE-ABS-KEY ("diabetes*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("hypertension") OR TITLE-ABS-KEY ("heart rate variability") OR TITLE-ABS-KEY (	4,445,123

item	Search input	result
	"heart attack") OR TITLE-ABS-KEY ("cardiopulmonary disease*") OR TITLE-ABS-KEY ("ischemic heart disease*") OR TITLE-ABS-KEY ("blood coagulation") OR TITLE-ABS-KEY ("deep vein thrombosis") OR TITLE-ABS-KEY (stroke) OR TITLE-ABS-KEY (morbidity) OR TITLE-ABS-KEY (" hospital admission*") OR TITLE-ABS-KEY ("outpatient visit*") OR TITLE-ABS-KEY (" emergency room visit*") OR TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (" DNA Methylation Change*") OR TITLE-ABS-KEY ("neurobehavioral function*") OR TITLE-ABS-KEY (" Inflammatory disease* ") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (abortion) OR TITLE-ABS-KEY ("Alzheimer's disease*") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (disability) OR TITLE-ABS-KEY ("cognitive function") OR TITLE-ABS-KEY ("Parkinson's disease*")	
#3	ALL (outdoor) AND ALL (" air pollution*")	31,240
#4	TITLE-ABS-KEY ("meta analysis*") OR TITLE-ABS-KEY ("systematic review*")	330,816
	#1 AND #2 AND #3 AND #4	**216**

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1. Database and time period

Web of science– inception-6/24/2018

2. Language:

English

3. Search strategy:

item	search	result
#1	TS = (Ozone* OR sulfur dioxide* OR carbon monoxide* OR nitrogen dioxide* OR PM2.5 OR PM10 OR total suspended particle* OR suspended particulate matter* OR Toxic air pollutant* OR volatile organic pollutant OR nitrogen oxide*)	674,294

item	search	result
#2	TS = (asthma OR lung cancer OR respiratory infection* OR respiratory disorder* OR diabetes OR chronic respiratory disease* OR chronic obstructive pulmonary disease* OR hypertension OR heart rate variability OR heart attack OR cardiopulmonary disease* OR ischemic heart disease* OR blood coagulation* OR deep vein thrombosis OR stroke OR morbidity OR hospital admission* OR outpatient visit* OR emergency room visit* OR mortality OR DNA methylation change* OR neurobehavioral function OR Inflammatory disease* OR skin disease* OR abortion OR Alzheimer's disease* OR disability OR cognitive function OR Parkinson's disease*)	7,157,410
#3	TS = (outdoor AND air pollution*)	10,814
#4	TS = ("meta analysis ")	174,699
	#1 AND #2 AND #3 AND #4	**53**
#5	TS = ("systematic review ")	163,736
	#1 AND #2 AND #3 AND #5	**33**

[a]: Database Cochrane search result was zero.

Supplemental Table S3:
Confidence result of identified studies.

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yang et al (2018) [27]	Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Zhao et al (2018) [28]	Ambient ozone exposure and mental health: A systematic review of epidemiological studies	Germany	General air pollution gas	Mental disorders	Medium
Newell et al (2018) [29]	Cardiorespiratory health effects of gaseous ambient air pollution exposure in low and middle income countries: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Health Records	Medium
An et al (2018) [30]	Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis	America	Mixed air pollution	Other diseases	Medium
Zhang, Wang & Lu (2018) [31]	Exposure to nitrogen dioxide and chronic obstructive pulmonary disease (COPD) in adults: a systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
DeVries, Kriebel & Sama (2017) [32]	Outdoor Air Pollution and COPD-Related Emergency Department Visits, Hospital Admissions, and Mortality: A Meta-Analysis	America	Mixed air pollution	Health Records	Medium
Khreis et al (2017) [33]	Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Fajersztajn et al (2017) [34]	Short-term effects of fine particulate matter pollution on daily health events in Latin America: a systematic review and meta-analysis	Brazil	Fine particulate matter	Health Records	Medium
Huang et al (2017) [35]	Relationship between exposure to PM2.5 and lung cancer incidence and mortality: A meta-analysis	China	Fine particulate matter	Health Records	Medium
Nguyen Thi Trang et al (2017) [36]	Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-series and case-crossover studies	Switzerland	Mixed air pollution	Respiratory diseases	Medium
Orellano et al (2017) [37]	Effect of outdoor air pollution on asthma exacerbations in children and adults: Systematic review and multilevel meta-analysis	Argentina	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Zhao et al (2017) [38]	The impact of short-term exposure to air pollutants on the onset of out-of-hospital cardiac arrest: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Achilleos et al (2017) [39]	Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis	America	Fine particulate matter	Health Records	Low
Ngoc et al (2017) [40]	Systematic review and meta-analysis of human skin diseases due to particulate matter	South Korea	Fine particulate matter	Other diseases	Medium
Lin et al (2017) [41]	Lung cancer mortality of residents living near petrochemical industrial complexes: a meta-analysis	China	Other toxic substances	Health Records	Medium
Froes Asmus et al (2016) [42]	A Systematic Review of Children's Environmental Health in Brazil	Brazil	Mixed air pollution	Respiratory diseases	Low
Zhang et al (2016b) [43]	Association between atmospheric particulate matter and adverse pregnancy outcomes in the population	China	Fine particulate matter	Pregnancy & children	Medium
Lim et al (2016) [44]	Short-term effect of fine particulate matter on children's hospital admissions and emergency department visits for asthma: A systematic review and meta-analysis	South Korea	Fine particulate matter	Respiratory diseases	Medium
Mills et al (2016) [45]	Distinguishing the associations between daily mortality and hospital admissions and nitrogen dioxide from those of particulate matter: A systematic review and meta-analysis	United Kingdom	General air pollution gas	Health Records	Medium
Fan et al (2016) [46]	The impact of PM2.5 on asthma emergency department visits: a systematic review and meta-analysis	China	Fine particulate matter	Health Records	Medium
Bloemsma, Hoek & Smit, 2016) [47]	Panel studies of air pollution in patients with COPD: Systematic review and meta-analysis	Netherlands	Fine particulate matter	Cardiovascular diseases	Medium
Li et al (2016) [48]	Major air pollutants and risk of COPD exacerbations: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Franchini et al (2016) [49]	Association between particulate air pollution and venous thromboembolism: A systematic literature review	Italy	Fine particulate matter	Cardiovascular diseases	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Pascal et al (2016) [50]	The mortality impacts of fine particles in France	France	Fine particulate matter	Health Records	Medium
Checa Vizcaino et al (2016) [51]	Outdoor air pollution and human infertility: a systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Power et al (2016) [52]	Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research	America	Mixed air pollution	Mental disorders	Medium
Song et al (2016) [53]	Short-term exposure to air pollution and cardiac arrhythmia: A meta-analysis and systematic review	China	Mixed air pollution	Cardiovascular diseases	Medium
Flores-Pajot et al (2016) [54]	Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: A review and meta-analysis	Canada	Mixed air pollution	Mental disorders	Medium
Hou et al (2016) [55]	The role of the PM2.5-associated metals in pathogenesis of child Mycoplasma Pneumoniae infections: a systematic review	China	Fine particulate matter	Respiratory diseases	Low
Zhang et al (2016a) [12]	Short-term exposure to air pollution and morbidity of COPD and asthma in East Asian area: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2016) [56]	Impact of air quality guidelines on COPD sufferers	America	Mixed air pollution	Cardiovascular diseases	Medium
Cai et al (2016) [57]	Associations of Short-Term and Long-Term Exposure to Ambient Air Pollutants With Hypertension: A Systematic Review and Meta-Analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Luo et al (2015) [58]	Short-term exposure to particulate air pollution and risk of myocardial infarction: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2015) [59]	Fine particle components and health - A systematic review and meta-analysis of epidemiological time series studies of daily mortality and hospital admissions	United Kingdom	Mixed air pollution	Health Records	Low
Hamra et al (2015) [60]	Lung cancer and exposure to nitrogen dioxide and traffic: A systematic review and meta-analysis	America	Mixed air pollution	Cancer	Low
Chen et al (2015) [61]	Traffic-related air pollution and lung cancer: A meta-analysis	China	Mixed air pollution	Cancer	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Jadambaa et al (2015) [62]	The impact of the environment on health in Mongolia: A systematic review	Mongolia	Mixed air pollution	Respiratory diseases	Low
Eze et al (2015) [63]	Association between ambient air pollution and diabetes mellitus in Europe and North America: Systematic review and meta-analysis	Switzerland	Mixed air pollution	Chronic diseases	Medium
Nurmatov et al (2015) [64]	Volatile organic compounds and risk of asthma and allergy: A systematic review	United Kingdom	Other toxic substances	Respiratory diseases	Low
Cui et al (2015) [65]	Ambient particulate matter and lung cancer incidence and mortality: A meta-analysis of prospective studies	China	Fine particulate matter	Health Records	Medium
Rodriguez-Villamizar et al (2015) [66]	The effects of outdoor air pollution on the respiratory health of Canadian children: A systematic review of epidemiological studies	Canada	Mixed air pollution	Respiratory diseases	Low
Bowatte et al (2015) [67]	The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: A systematic review and a meta-analysis of birth cohort studies	Australia	Mixed air pollution	Respiratory diseases	Medium
Shah et al (2015) [68]	Short term exposure to air pollution and stroke: Systematic review and meta-analysis	United Kingdom	Mixed air pollution	Cardiovascular diseases	Medium
Scheers et al (2015) [69]	Long-Term Exposure to Particulate Matter Air Pollution Is a Risk Factor for Stroke: Meta-Analytical Evidence	Belgium	Fine particulate matter	Cardiovascular diseases	Medium
Filippini et al (2015) [70]	A review and meta-analysis of outdoor air pollution and risk of childhood leukemia	Italy	Mixed air pollution	Cardiovascular diseases	Low
Frutos et al (2015) [71]	Impact of air pollution on fertility: A systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Zheng et al (2015) [9]	Association between Air pollutants and asthma emergency room visits and hospital admissions in time series studies: A systematic review and meta-Analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2015) [72]	Association of exposure to particular matter and carotid intima-media thickness: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Balti et al (2014) [73]	Air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis	South Africa	Mixed air pollution	Chronic diseases	Medium
Faustini, Rapp & Forastiere (2014) [74]	Nitrogen dioxide and mortality: Review and meta-analysis of long-term studies	Italy	Mixed air pollution	Health Records	Medium
Li et al (2014) [75]	Mechanisms in endocrinology: Main air pollutants and diabetes-associated mortality: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Rossignol, Genuis & Frye (2014) [76]	Environmental toxicants and autism spectrum disorders: A systematic review	America	Other toxic substances	Mental disorders	Low
Hamra et al (2014) [77]	Outdoor particulate matter exposure and lung cancer: A systematic review and meta-analysis	France	Fine particulate matter	Cancer	Low
Hu et al (2014) [78]	Ambient air pollution and hypertensive disorders of pregnancy: A systematic review and meta-analysis	America	Mixed air pollution	Cardiovascular diseases	Medium
Pedersen et al (2014) [79]	Ambient air pollution and pregnancy-induced hypertensive disorders: A systematic review and meta-analysis	Spain	Mixed air pollution	Cardiovascular diseases	Medium
Bell, Zanobetti & Dominici (2014) [80]	Who is more affected by ozone pollution? A systematic review and meta-analysis	America	General air pollution gas	Health Records	Low
Shin et al (2014) [81]	Outdoor fine particles and nonfatal strokes: Systematic review and meta-analysis	America	Fine particulate matter	Cardiovascular diseases	Low
Song et al (2014) [82]	The global contribution of outdoor air pollution to the incidence, prevalence, mortality and hospital admission for chronic obstructive pulmonary disease: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2014) [83]	Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: A systematic review and meta-analysis	United Kingdom	Fine particulate matter	Health Records	Low
Dick et al (2014b) [84]	A systematic review of associations between environmental exposures and development of asthma in children aged up to 9 years	United Kingdom	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yamamoto, Phalkey & Malik (2014) [85]	A systematic review of air pollution as a risk factor for cardiovascular disease in South Asia: Limited evidence from India and Pakistan	Germany	Mixed air pollution	Cardiovascular diseases	Medium
Chen et al (2014) [86]	Effects of air pollution on the risk of congenital anomalies: A systematic review and meta-analysis	France	Mixed air pollution	Mental disorders	Medium
Dick et al (2014a) [15]	Associations between environmental exposures and asthma control and exacerbations in young children: A systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Teng et al (2014) [87]	A systematic review of air pollution and incidence of out-of-hospital cardiac arrest	Australia	Mixed air pollution	Cardiovascular diseases	Low
Vawda et al (2014) [88]	Associations between inflammatory and immune response genes and adverse respiratory outcomes following exposure to outdoor air pollution: A huge systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Low
Yu et al (2014) [89]	Short-term effects of particulate matter on stroke attack: Meta-regression and meta-analyses	China	Fine particulate matter	Cardiovascular diseases	Medium
Liang et al (2014) [90]	Effect of exposure to PM2.5 on blood pressure: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Zhu et al (2013) [91]	The relationship between particulate matter (PM10) and hospitalizations and mortality of chronic obstructive pulmonary disease: A meta-analysis	China	Fine particulate matter	Health Records	Low
Hoek et al (2013) [92]	Long-term air pollution exposure and cardio-respiratory mortality: A review	Netherlands	Fine particulate matter	Health Records	Medium
Anderson, Favarato & Atkinson (2013a) [93]	Long-term exposure to outdoor air pollution and the prevalence of asthma: Meta-analysis of multi-community prevalence studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Anderson, Favarato & Atkinson (2013b) [94]	Long-term exposure to air pollution and the incidence of asthma: Meta-analysis of cohort studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Bell, Zanobetti & Dominici (2013) [95]	Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis.	America	Fine particulate matter	Other diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Nieuwenhuijsen et al (2013) [96]	Environmental risk factors of pregnancy outcomes: a summary of recent meta-analyses of epidemiological studies.	Spain	Fine particulate matter	Pregnancy & children	Medium
Mehta et al (2013) [97]	Ambient particulate air pollution and acute lower respiratory infections: A systematic review and implications for estimating the global burden of disease	America	Mixed air pollution	Respiratory diseases	Medium
Park, Bae & Hong (2013) [98]	PM10 exposure and non-accidental mortality in Asian populations: A meta-analysis of time-series and case-crossover studies	South Korea	Fine particulate matter	Health Records	Medium
Stieb et al (2012) [99]	Ambient air pollution, birth weight and preterm birth: A systematic review and meta-analysis	Canada	Mixed air pollution	Pregnancy & children	Medium
Gasana et al (2012) 100	Motor vehicle air pollution and asthma in children: A meta-analysis	America	Mixed air pollution	Respiratory diseases	Medium
Li et al (2012) [101]	Meta-Analysis of Association between Particulate Matter and Stroke Attack	China	Fine particulate matter	Cardiovascular diseases	Medium
Takenoue et al (2012) [8]	Influence of outdoor NO2 exposure on asthma in childhood: Meta-analysis	Japan	General air pollution gas	Health Records	Medium
Tashakkor, Chow & Carlsten, 2011) [102]	Modification by antioxidant supplementation of changes in human lung function associated with air pollutant exposure: A systematic review	Canada	Other toxic substances	Respiratory diseases	Low
Afshari et al (2011) [103]	Inhaled nitric oxide for acute respiratory distress syndrome and acute lung injury in adults and children: A systematic review with meta-analysis and trial sequential analysis	Denmark	Other toxic substances	Other diseases	Medium
Shah, Balkhair & Knowledge Synth Grp Determinants (2011) [104]	Air pollution and birth outcomes: A systematic review	Canada	Mixed air pollution	Pregnancy & children	Low
Forbes et al (2009) [105]	Chronic exposure to outdoor air pollution and diagnosed cardiovascular disease: meta-analysis of three large cross-sectional surveys.	United Kingdom	General air pollution gas	Cardiovascular diseases	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Mahjub & Gh (2006) [106]	Meta-analysis of case-referent studies of specific environmental or occupational pollutants on lung cancer	Iran	Mixed air pollution	Cancer	Medium
Ito, De Leon & Lippmann (2005) [107]	Associations between ozone and daily mortality: Analysis and meta-analysis	America	General air pollution gas	Health Records	Low
Ward & Ayres (2004) [108]	Particulate air pollution and panel studies in children: a systematic review.	United Kingdom	Fine particulate matter	Respiratory diseases	Low

BMJ Open

Exposure to outdoor air pollution and its human-related health outcomes: an evidence gap map

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031312.R1
Article Type:	Original research
Date Submitted by the Author:	08-Oct-2019
Complete List of Authors:	sun, zhuanlan; Tongji University, Zhu, Demi; Shanghai Jiaotong University
Primary Subject Heading:	Health policy
Secondary Subject Heading:	Health policy
Keywords:	outdoor air pollution, health outcomes, evidence gap map

Exposure to outdoor air pollution and its human-related health outcomes: an evidence gap map

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ABSTRACT

Objectives Outdoor air pollution is a serious environmental problem worldwide. Current systematic reviews and meta analyses mostly focused on some specific health outcomes or some specific air pollution. This evidence gap map (EGM) is to identify existing gaps from systematic reviews (SRs) and meta analyses (MAs) and report them in broad topic areas.

Design and Setting SRs and MAs investigating the impact of outdoor air pollution on human health outcomes were collected. PubMed, Cochrane, Scopus, and Web of Science, were searched from their inception until June 2018. Citations and reference list were traced. Two reviewers screened the titles and abstracts independently following the predefined eligibility inclusion criteria. Characteristics of the included SRs and MAs were extracted and summarised.

Participants Europe, Asia and North America published 93% of SRs and MAs included in this EGM. 31% of the SRs and MAs (27/86) included primary studies that conducted in 5-10 countries and nearly 30% was unclearly reported. Publication trends of them is increasing in recent 10 years. A total of 2,864 primary studies were included. The median number of included primary studies was 20 (range, 7-167). Cohort studies, case-crossover studies and time series studies are the top 3 mostly used study design.

Primary and secondary outcome measures EGM was used to visually display outdoor air pollution, health outcomes, literature size, and a broad strength of findings.

Results The mostly researched population is the group of all ages (46/86, 53%). Cardiovascular diseases, respiratory diseases, and health service records are mostly reported. Lack of uniform diagnostic criteria of diseases, unclearly reporting of air pollution exposure and time period of primary studies are main research gaps.

Conclusions This EGM provided a visual overview of health outcomes affected by outdoor air pollution exposure. Future researches should focused on chronic diseases, cancer and mental disorders.

Strengths and limitations of this study

This evidence gap map focused on a broad range of air pollution and human health outcomes based on a systematic search of four databases from their inception until June 2018.

Only systematic reviews and meta analyses were included in this evidence gap map.

This evidence gap map identified some evidence gaps, and future research needs specifically focused on clearly reporting of diagnostic criteria of diseases, exposure of air pollution and time period.

The bubble plot was used to visualizing the evidence gap, the color represented the confidence of included systematic reviews and the size indicated the number of included systematic reviews.

The publication language of included systematic reviews and meta analyses was restricted in English, thus possibly missing pertinent information written in other languages.

INTRODUCTION

Outdoor air pollution, a serious environmental problem and major concern of public health worldwide, has caused approximately 4.2 million global deaths in 2016.[1] It is a severe invisible killer posing serious human health hazards, especially in developing countries where the industrialization and urbanization developed quickly.[2] There are many common types of air

pollutants, such as fine particulate matter ($PM_{2.5}$, PM_{10}), ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_2 and NO_x), volatile organic pollutants and some other toxic air pollutants. The human-related health outcomes affected by such air pollutants have been studied for decades. Researchers from various disciplines all over the world have shown constant interest in health effects of outdoor air pollution, such as cardiovascular disease, respiratory disease, cancer, Alzheimer's disease and so on.[3–6]

Systematic reviews (SRs) aim to synthesis all relevant high quality evidence on a specific topic in terms of the health outcomes of outdoor air pollution.[7] It was reported that outdoor NO_2 exposure triggered asthma,[8,9] other studies identified human mortality was positively associated with $PM_{2.5}$ exposure.[10,11] However, many studies focused on interactive effects with regard to several types of health outcomes affected by various air pollutants,[12,13] and there are some overlapping SRs conducted on the same topic implied inconsistent results.[14,15] The specific topic of SRs findings on particular factors cannot be used to provide a comprehensive overview of air pollution related health outcomes.

To overcome this barrier, some novel knowledge synthesis approaches (e.g., scoping review, systematic mapping, evidence mapping etc.) have been developed to evaluate the overall effect of evidence on a broader area, highlighting both current knowledge and gaps in evidence.[16–19] Evidence gap map (EGM), an emerging synthesis method, was proposed to systematically and comprehensively assess intervention effects and outcomes in a user-friendly two-dimensional matrix framework. It can also visualize the existing evidence in a map with critical quality appraisal for policy and research implications.[20,21]

EGM can inform a strategic approach to build the evidence based on particular issues. Water, sanitation and hygiene interventions were evaluated by 3ie to inform policy decision and address evidence gap.[21] 3ie, known as the International Initiative for Impact Evaluation, is a global collaboration focused on evidence synthesis. To our knowledge, there are few researches use EGM to present the evidence visually on outdoor air pollution exposure related health outcome topics.

We constructed an EGM on the health effects of outdoor air pollution by comprehensively summarizing existing SRs and meta-analyses (MAs). The main purpose of this EGM was to identify the evidence gaps for potential research prioritization. In addition, it also can be used in the evidence-based environmental policymaking supporting.

MATERIALS & METHODS

EGM is a newly developed knowledge synthesis methods, which is similar to evidence mapping. There is no standard methodology guideline available for evidence mapping currently.[22] We followed the methodology framework presented by Snilstveit et al to conduct this EGM.[21] Establishing the framework was divided into six steps: developing scope; setting inclusive

criteria; searching relevant studies; selecting studies; extracting data and appraising quality; and summarizing results.

Scope development

The established framework was two-dimensional matrix of outdoor air pollution and health outcomes. It derived from the major policies of interest and existing academic literatures. The row and column of the array included all categories of outdoor air pollution and human-related health outcomes respectively.

A consultation with key stakeholders, including academic researchers, policymakers, practitioners and funders were involved to make sure the acceptance of the framework. The consultation was carried out at the process of study inclusion, literature search and data extraction. All the key stakeholders were invited to take part in the consultation to determine the scope and the technologies of the EGM.

Study inclusion criteria

We followed 3ie's guideline to include systematic review and meta-analysis studies and to summarise all the available evidence on human-related health outcomes affected by particular air pollution.[23]

Study search

Four electronic databases, PubMed, Cochrane, Scopus, and Web of Science, were searched from their inception until June 2018. The language was restricted to English. We compiled a list of outdoor air pollution and health outcome terms by reviewing the potential text words in the titles or abstracts of the most pertinent literatures (supplemental table s1), this process was conducted by consulting with experts who are members of the Committee on Public Health and Urban Environment Management in China. We then used advanced database search strategies on key words, combined with Boolean operators (AND, OR, NOT) and wild card symbols (*), so as to search for the potentially relevant literatures (supplemental table s2). To prevent any relevant literature from missing, we subsequently traced citations and reference list of literatures to generate more relevant systematic review and meta-analysis studies.

Inclusion assessment

Table 1 Inclusion and exclusion criteria used in this EGM for eligible studies

Inclusive criteria	Exclusive criteria
Studies types	**Studies type**
SRs and MAs	Indoor air pollution
Studies methods	Primary studies
Quantitative SRs	**Studies methods**
Studies conclusion	Qualitative reviews only
Data supported outcome relevant to outdoor air pollution	

SRs, systematic reviews; MAs, meta-analyses.

The first step of inclusion assessment involved screening the titles and abstracts of SRs and MAs by two reviewers independently. The inclusion and exclusion criteria for EGM were discussed by

the team members at the beginning of this process (table 1). Primary studies, such as observational study, time series study and causal inference study, were not included. The definition of outdoor air pollution is that exposure take place outside of the built environment. Both the health outcome and outdoor air pollution reported in the SRs and MAs are eligible. Reference management software Mendeley was used to systematically remove duplicated literatures and assess potential literatures that meet the inclusion criteria.

The second step of the study selection stage was the full text retrieve of all potentially eligible articles, which was independently screened by the two reviewers as well. If disagreements occurred between them, a third specialist made the final decision.

Data extraction and critical appraisal

Characteristics of the included SRs and MAs were extracted and summarized by one reviewer and checked for accuracy by the other. Extracted data included authors, publication year, the location of corresponding author(s), publication journal discipline, study design, study duration, sample size, study region, target population, types of air pollution, and health outcomes (table 2). Other categories, such as key results, will extract based on the advice from some researchers from public health and policymakers. We categorized the results of health outcomes into three parts: positive, negative and ambiguous. Positive represents air pollution has harmful effects on human health outcome. Negative means no harmful effect was found in the MAs. Air pollution was categorized as: general air pollution gas, fine particulate matter, other toxic substances and combinations of multiple pollutants. The definition of "combinations of multiple pollutants" is the mixture of two or more air pollutants as followings: O_3, SO_2, CO, NO_2, $PM_{2.5}$, PM_{10}, suspended particulate matter, and total suspended particle.

Table 2 Information to be collected during the data extraction stage

Study design	Study population	Exposures	Outcome information
Author(s)	Sample size	Air pollution	Health outcomes
Publication Year	Study region		Key results
The location of corresponding author(s)	Target population		
Discipline of journal a			
Study design			
Study duration			

a: The discipline catalog is from Journal Citation Report published by Web of Science.

The potential study designs and the inherent characteristics (strengths and limitations) of each design make the quality assessment complex.[24] We applied the Supporting the Use for Research Evidence (SURE) checklist to appraise the quality of included SRs and MAs in terms of the confidence, [21] rating them as high, medium or low confidence.[20] SURE is a mechanism aims to strengthen the evidence-informed policymaking, which is more appropriate for our research. SURE checklist was designed to assess three dimension of the included SRs and MAs: (1) methods used to identify, include and critically appraise studies, (2) methods used to analysis the findings, and (3) overall assessment of the reliability of the review. Two authors

independently assessed the quality of the included SRs and MAs. Any difference will be resolved by consulting with a third researcher.

Summarization and visualization

To provide a snapshot of what it is known and where evidence is lacking, a bubble plot was used to represent extend of health outcomes affected by outdoor air pollution. We followed the visual representation of 3ie's two-dimensional framework to generate the bubble plot. [21] In the EGM plot, traffic light color indicates three levels of findings' confidence, which assessed by using the SURE checklist. Red bubbles represent low confidence, yellow ones represent medium, and green ones represent high confidence. Bubbles size represents the quantity of corresponding SRs and MAs.

Patient and public involvement

No patient or public involved in this EGM.

RESULTS

Figure 1 displayed the systematic literatures search process for EGM. Literature search of four electronic databases yielded 361 potentially relevant studies. After removing duplicate researches, 266 unique studies were collected. Based on screening the titles and the abstracts, there were 118 SRs and MAs were assessed as being relevant. To avoid missing potential studies, we also manually searched the relevant studies in the top five impact factor periodicals, which were chosen in the collection of our included published SRs and MAs. Tracing of citations and reference lists made that 5 more relevant studies were included at the end of this process. In total, 123 SRs and MAs were included in the full-text screening analysis. Finally, 86 eligible articles were included in our EGM. In all 86 SRs and MAs, a total of 2,864 original studies were included. The median number of original studies was 20 (range, 7-167); the variance value of which was 31.99.

General descriptions summary of included SRs and MAs

Of the 86 included SRs and MAs, most of them were published in Europe, Asia and North America, with the proportion of 37%, 34% and 22% respectively (table 3). As illustrated in figure 2, the SRs and MAs published in the top three continents were concentrated in a small group of countries, with China, USA, and UK on the top of the list. Little evidences came from Africa, Australia, and South America, with an overall proportion of only 6%. The distribution of publication is unbalanced.

The population of included SRs and MAs were categorized into seven subgroups: infants, children and adolescents, adults, women and pregnancy, all ages, elderly, and not specified (table 3). The largest population affected by outdoor air pollution fell under the group of all ages (46/86; 53%), followed by the group of children and adolescents under the age of 20, with the percentage of 17% (15/86). The infants and elderly groups shared only 2%, however, these two groups of people are the most affected by air pollution.

Almost half of the available primary studies included in SRs and MAs were conducted in more than 5 countries. 21% of the SRs and MAs only included primary studies conducted less than 5 countries. The samples size of the primary studies included in the SRs and MAs varied with a wide range, the number of which ranged from less than one hundred to millions (range: 83-11,850,884 participants).

Table 3 General descriptions for included SRs and MAs

(n=86)	N	%		N	%
Continent [a]			**Numbers of original study**		
Africa	1	1%	<10 studies	10	12%
Australia	2	2%	10~30 studies	46	53%
South America	3	3%	30~60 studies	13	15%
North America	19	22%	>60 studies	13	15%
Asia	29	34%	Not clearly mentioned	4	5%
Europe	32	37%	**Study period**		
Countries of primary studies included in SRs and MAs			<10 years	11	13%
<5 countries	18	21%	10 ~ 20 years	23	27%
5 ~ 10 countries	27	31%	> 20 years	7	8%
10 ~ 20 countries	15	17%	Not clearly mentioned	45	52%
> 20 countries	1	1%	**Types of study design**		
Not clearly mentioned [b]	25	29%	Single	13	15%
Population			Multiply	73	85%
Infants	2	2%	**Study design**		
Children & Adolescents	15	17%	Cohort	41	
Adults	7	8%	Case-crossover	27	
Elderly	2	2%	Time-series	25	
Women & Pregnancy	4	5%	Case-control	24	
All ages	46	53%	Cross-sectional	20	
Not specified	10	12%	**Sample size(range)**	(83-11,850,884)	

SRs and MAs, systematic reviews and meta-analyses.

Of the study design, 15% (13/86) of the included SRs and MAs were conducted by using single study design, the rest 73 SRs and MAs originated from primary studies with multiply study designs. The top five mostly used study designs of the primary studies included in the SRs and MAs were cohort, case-crossover, time-series, case-control, and cross-sectional, the corresponding number were 41, 27, 25, 24, and 20 respectively. The time period, which means the publication date intervals of primary studies included in the SRs and MAs, were mostly (51%) unclearly reported.

Publication trends of included SRs and MAs

The included SRs and MAs were mainly conducted in six research fields. As the cumulative frequency trend chart displayed in figure 3, the number of the SRs showed an increasing trend from 2004 to 2018. Most of the included SRs and MAs were published in the recent six years, with no SRs published before the year 2004. All included SRs and MAs were categorized by according to the journals of publication by using the Journal Citation Report in Web of science

database. There was an increasing trend in the number of publications in the fields of medicine and public environmental occupational health from 2004 to 2013, and the trend remarkably raised from 2013 till now, especially in medicine researches. The environmental sciences saw a rising trend since 2011, then the trend spiked up in the years of 2012 and 2015 respectively, and reached its peak number in 2017. Three disciplines, including environmental sciences and public environmental occupational health, multidisciplinary, and neurosciences, increased smoothly since the year 2011.

Summary by health outcome groups

We categorized health outcomes into eight groups based on the specialists' suggestions: cardiovascular diseases, chronic diseases, health service records, cancer, mental disorders, respiratory diseases, pregnancy and children, and other diseases, which are important features of the EGM visualization. The categorized list of health outcomes was showed in table 4.

Table 4 The categorized list of health outcomes

Health outcome groups	Health outcome of inclusive studies
Respiratory diseases	Asthma, respiratory diseases, ALRI
Chronic diseases	Diabetes
Cardiovascular diseases	Hypertension, BP, COPD,OHCA,VTE,CVD, myocardial infarction, Arrhythmia , stroke
Health service records	Morbidity, hospital admissions, ED visits, mortality
Cancer	Lung cancer
Pregnancy & Children	Fertility, pregnancy, Birth
Mental disorders	Mental health, cognition, ASD
Other diseases	Physical inactivity, skin disease, health risks

ALRI, acute lower respiratory infections; BP, blood pressure; COPD, chronic obstructive pulmonary disease; OHCA, out-of-hospital cardiac arrest; VTE, venous thrombo embolism; CVD, cardiovascular diseases; ED, emergency department; ASD, autism spectrum disorder.

The inclusive studies in our EGM were summarized based on health outcome groups (table 5). The information of the types of air pollution, number of primary studies, population group, sample size, and key results were included in the table 5. Of the 86 identified SRs and MAs, 24 studies reported cardiovascular diseases as outdoor air pollution related health outcomes, the figures of health service records and respiratory diseases studies that had been reported as an adverse effect of outdoor air pollution exposure were 22 and 19 respectively. Each of the rest five groups of health outcomes accounted for an average SRs and MAs of 4. All SRs and MAs included more than 10 primary studies at least, health outcomes in all ages account for the largest groups in all categories, expect for those of respiratory diseases category, in which children was the most suffered ones.

Overall, combinations of multiple pollutants was the dominant type of outdoor air pollution, which tended to show a positive harmful effect in all health outcome groups. What's more, it was the main cause of the respiratory diseases among children and the chronic diseases among people in all ages.

EGMs visualization

The feature of EGMs is to provide a visual display of evidence from the SRs and MAs. Bubble plot was used to display the types of air pollution and related health outcomes in a two dimensional matrix framework, as presented in figure 4. The colors of bubble in the map represent the confidence of SRs and MAs, which is assessed by SURE checklist.[25] Red color of bubble represents low confidence and yellow color of bubble means medium confidence. The sizes of bubble indicate the relative number of included studies, a larger bubble represents a larger study sample size in each grid. Confidence result of identified studies were showed in supplemental table s3. There is no green bubble in our EGM, which means the high-quality SRs and MAs are in urgent need. What's more, there is a correlation between the study sample size and the research quality.

Table 5 Characteristics of included SRs and MAs based on health outcome groups

Health outcome group (number of SRs and MAs)	Types of air pollution [a] (number of SRs and MAs)	Number of primary studies (mean +/- STD)	Population group (number of SRs and MAs)	Sample size (range)	Key results
Cardiovascular diseases (24)	Fine particulate matter (10) General air pollution gas (1) combinations of multiple pollutants (13)	32 +/- 30	Infant & children (1) Adults & old (5) All ages (16) Other (2)	（83, 11,850,884）	Positive (22) Ambiguous (2)
Chronic diseases (2)	combinations of multiple pollutants (2)	11 +/- 2	All ages (2)	（402, 62,012）	Positive (2)
Health service records (22)	Fine particulate matter (10) General air pollution gas (4) Other toxic substances (1) Mixed air pollution (7)	40 +/- 38	Infant & children (1) Adults & old (1) All ages (15) Other (5)	（1,050, 50,756,699）	Positive (21) Negative (1)
Cancer (4)	Fine particulate matter (1) combinations of multiple pollutants (3)	24 +/- 10	Adult (1) All ages (3)	（29, 500,000）	Positive (4)
Mental Disorders (5)	General air pollution gas (1) Other toxic substances (1) Mixed air pollution (3)	16 +/- 10	Infant & children (2) All ages (2) Other (1)	（252, 7,203）	Positive (3) Negative (1) Ambiguous (1)
Respiratory diseases (19)	Fine particulate matter (3) Other toxic substances (1) combinations of multiple pollutants (15)	37 +/- 31	Infant & children (11) Adults & old (1) All ages (6) Other (1)	（186, 1,146,215）	Positive (18) Negative (1)
Pregnancy & children (6)	Fine particulate matter (2) combinations of multiple pollutants (4)	23 +/- 22	Infant & children (1) All ages (3) Other (2)	（263, 3,545,177）	Positive (6)
Other diseases (4)	Fine particulate matter (2) Other toxic substances (1) combinations of multiple pollutants (1)	35 +/- 48	Adults & old (1) All ages (2) Other (1)	（73, 2,381,292）	Positive (3) Negative (1)

SRs and MAs, systematic reviews and meta-analyses.

combinations of multiple pollutants is the mixture of two or more air pollutants as followings: O3, SO2, CO, NO2, PM2.5, PM10, suspended particulate matter, and total suspended particle.

DISCUSSION

This EGM provided the most up-to-date SRs and MAs by using the user-friendly visualization of the existing evidence in a matrix format of interventions and outcomes framework, so that it helps to set potential research agenda and promote evidence-based policy makings. EGM is novel evidence synthesized method in that they offer a reliable means of covering a broad scope of a particular sector, focusing on visualizing quality of the existing evidence in a user-friendly

format. Most importantly, EGM can address evidence gaps for funding research with limited resources and provide evidence-based information to support precise policy-making.

Most studies reported the health outcomes of cardiovascular diseases, respiratory diseases, and health service records, which were mainly affected by fine particulate matter or combinations of multiple pollutants. While little studies investigated other toxic substances and its adverse effect on human-related health outcomes. By identifying the evidence gaps that existed in the outdoor air pollution related health outcomes, more potential research agenda need to focus on chronic diseases, cancer and mental disorders, so that research gaps can be filled and evidence-based information can be provided to support precise policy-making. By highlighting the confidence of the existing evidence based on inclusive studies, policymakers can promote relevant policies based on the existing summarized evidences of outdoor air pollution related health outcomes. In addition, more high-quality SRs and MAs, primary studies and synthesized evidence across a range of disciplines are needed to ensure the confidence of existing evidence for the policy decision making.

This EGM is to comprehensively collect and category a variety body of SRs and MAs to overview the health outcomes affected by outdoor air pollution. However, the quality of 86 included SRs and MAs are either medium or low. The visualized categories of outdoor air pollution and health outcomes reveals the research gaps and concentrations of the existing literatures. The health outcomes mostly studied in outdoor air pollution researches often concentrate on cardiovascular diseases, respiratory diseases and health service records, including chronic obstructive pulmonary disease (COPD), blood pressure (BP), hypertension, asthma, morbidity, and mortality. These diseases are the most impactful in both researchers and ordinary people. The major air pollution types are fine particulate matter ($PM_{2.5}$, PM_{10}) and general air pollution gas (CO, SO_2, NO_2, and O_3), few health outcome studies was caused by other toxic air pollutants. These measurements of air pollutants, as air quality standards developed by U.S. government in 1970s, sometimes measured in different methods in other countries, which will induce some bias. Well-designed primary studies and meta-analyses on chronic diseases, cancer, especially metal disorders are needed. People with chronic diseases, such as diabetes or COPD, were more susceptible to air pollution. These chronic diseases are also age related. The health outcomes of these patients affected by air pollution are worthy of investigation.

There are some research gaps have been explored in this EGM. A major gap observed is lack of uniform diagnostic criteria of diseases. Criteria and reporting of air pollution related health outcomes were notably variable, with significant potential for subject heterogeneity. Future researches should define and report the diagnostic criteria more precisely. What's more, there is a difficulty in estimating the personal exposure of air pollution. The heterogeneity of air pollution exposure levels, which are both in the primary studies and meta analyses, may probably lead the "exposure bias". Although more and more primary studies began to use the measurement of

exposure time, there is still room to use more precise estimation, such as wearable sensor application. Another research gap we found is that the studies' period of SRs was not clearly reported. The air pollution levels are different in different time periods. Even in the same country or region, the levels of industrialization and modernization are different, which make air pollution effects different. These SRs and MAs should be updated, and the time period of SRs and MAs should also be clearly reported. "Population bias" gap was also found in our EGMs. When including more children, for example, it could have overestimated the true prevalence of the disease. Clearly stratified analysis of different age groups is needed for the reason that outdoor air pollution has different impacts on different age groups.

Some important areas of air pollution research are left blank in the EGM. For example, few of the SRs included healthcare costs related to outdoor air pollution. As the public focus on environmental sustainability become even stronger in recent years, the demand for studies may increase. Moreover, they should come as a warning to policymakers as it shows that actual evidence for the healthcare costs related to outdoor air pollution. More precisely, studies aimed at economic burden of outdoor air pollution are needed.

Most included SRs and MAs estimated the health outcomes affected by outdoor air pollution in general population rather than those with established disease, thus, summarization of the existing body of evidence should therefore be viewed in more researches that aim at evaluate the health outcomes of established disease affected by outdoor air pollution. Besides, researches focus on the physiological effects, such as increased heart rate and feelings of anxiety, are indispensable so that EGM can capture a comprehensive overview of air pollution related health outcomes. Geographically, it is worth noting that most of the available primary studies included in SRs and MAs were conducted in Western countries, where the median $PM_{2.5}$ concentration is less than 20 $\mu g/m^3$. In developing countries (such as China and India), however, the $PM_{2.5}$ concentrations in urban cities are likely to be up to $100\mu g/m^3$, which have made a great impact on the local environment and people's health outcomes. The location of the primary study is an impact factor related with the air pollution, and it should be considered with caution in both epidemiological study and systematic review. There is room for more robust impact evaluation in the process of systematic review by using subgroup analysis.

There have some research gaps in current research of air pollution effect on people health outcomes. Uniform diagnostic criteria of diseases, timely updating well design primary studies in local countries, and rational sampling (elders, children and patients with chronic diseases) should be considered with caution in the process of evidence-based policy decision making. These factors will affect the research outcomes by inducing some unobserved bias.

Limitations

Our EGM built on the evidence base from significant numbers of SRs and MAs that have quantitatively addressed the health outcomes influenced by air pollution. The "gold standard"

restriction on included studies may neglect important information available from studies. Since the main purpose of our EGMs is to provide a resource for policymakers, only inclusion of SRs and MAs is sufficient to generate reliable conclusions for policymakers.[20] Hundreds of quality appraisal methods exist in the synthesis knowledge studies,[26] the efficiency of these studies depend largely on the quality assessment result, we only applied SURE checklist instead of other quality assessment methods in that it is more suitable for EGMs. Two reviewers assessed separately to prevent any bias occurred.

Only English-language SRs and MAs were in included in our EGM, thus possibly missing pertinent information written in other languages. Primary studies, such as observational study, time series study and causal inference study, were not included in our EGM for the reason that systematic level evidence have been comprehensively collected the current researches. In addition, this EGM largely relied on information provided by included SRs and MAs, there may have been undetected errors of data abstraction or synthesis in one or more of the SRs. Finally, research gaps identified in this EGM do not necessarily equate to research needs. It should consider that the desirability, feasibility, and importance of the research gaps, highlighting the importance of stakeholder engagement in this process.

CONCLUSIONS

This EGM provided a visual overview of health outcomes affected by outdoor air pollution. Despite the outlined limitations, it is a useful tool to inform environmental policy decision makers. It also can promote further potential researches by visualizing and synthesizing high-quality SRs and highlighting the absolute gaps. More prospective studies, with large numbers of participants, are needed in developing countries. It will helpful to assess the long-term effects of air pollution more precisely.

Contributorship statement Zhuanlan Sun formulated the research question. Demi Zhu and Zhuanlan Sun devised the search strategy, consulting with experts from Committee on Public Health and Urban Environment Management in China. Demi Zhu and Zhuanlan Sun conducted the search, screened all titles, abstracts and full articles and extracted data. Demi Zhu and Zhuanlan Sun co-wrote the manuscript.

Competing interests None declared.

Funding This work was supported by a major projects of the National Social Science Fund of China grant number 13&ZD176.

Data sharing statement All data relevant to the EGM are included in the manuscript.

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FIGURE LEGEND

Figure 1 Systematic literatures search process for eligible SRs and MAs. SRs, systematic reviews; MAs, meta analyses.

Figure 2 Regions and countries distribution of eligible SRs and MAs.

The data of regions and countries are based on the information of corresponding authors. SRs, systematic reviews; MAs, meta analyses.

Figure 3 Numbers of inclusive eligible SRs and MAs in six research fields between 2004 and 2018.

The number of the eligible SRs and MAs saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years. SRs, systematic reviews; MAs, meta analyses.

Figure 4 EGM for health outcomes affected by outdoor air pollution. The colors of bubble represent the confidence of included SRs and MAs, red color represents low confidence and yellow color represents medium confidence. The sizes of bubble indicate the relative number of included SRs and MAs, and a larger bubble represents a larger study sample size in each grid. SRs, systematic reviews; MAs, meta analyses.

TABLE LEGEND

Table 1 Inclusion and exclusion criteria used in this EGM for eligible SRs and MAs.

Table 2 Information to be collected during the data extraction stage.

Table 3 General descriptions for included SRs and MAs..

Table 4 The categorized list of health outcomes.

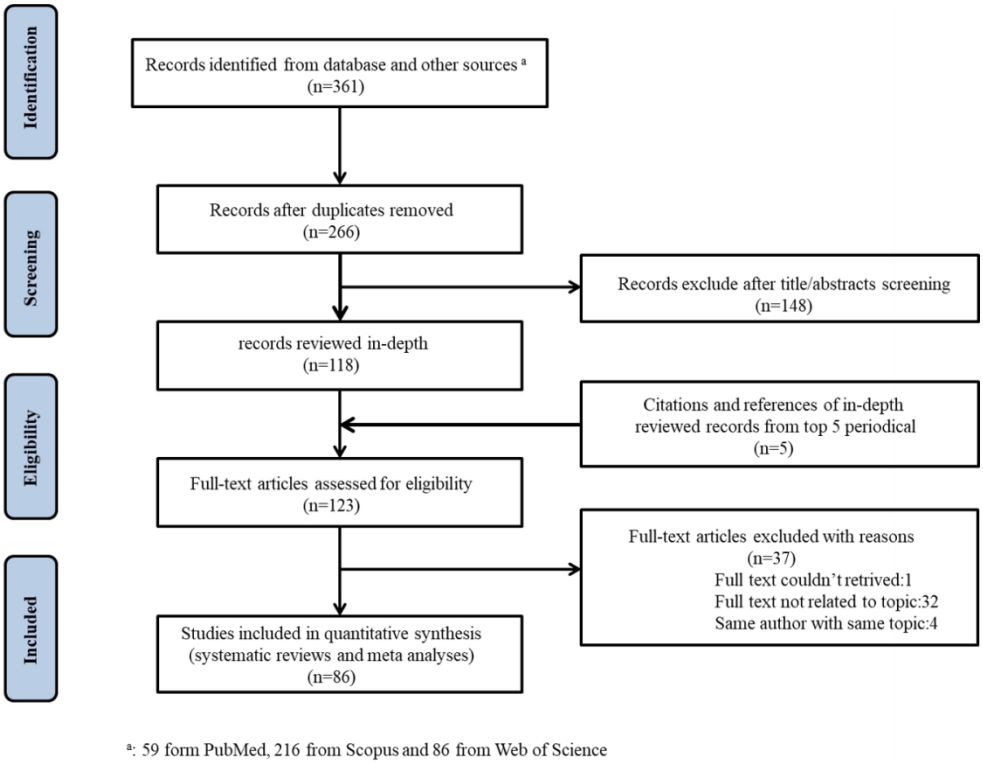
Table 5 Characteristics of included studies based on health outcome groups.

Supplemental Table S1 List of outdoor air pollution and health outcome related terms.

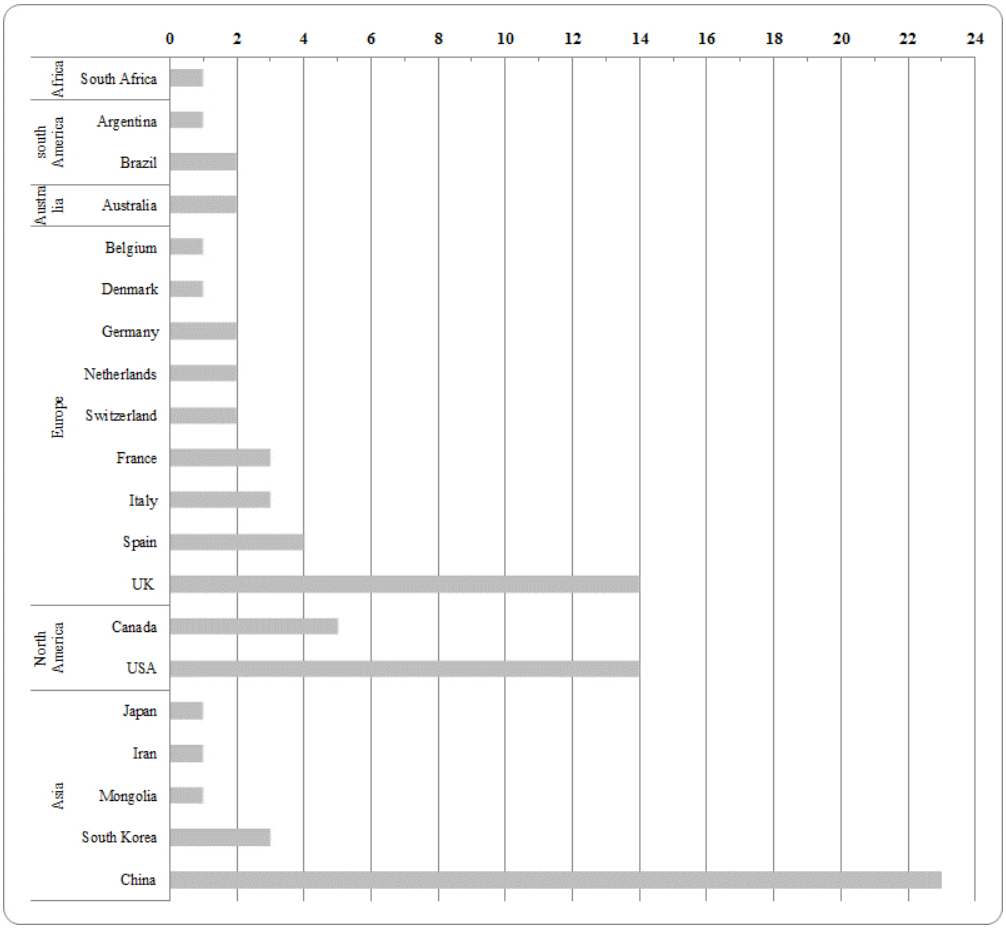
Supplemental Table S2 Search strategies for the potentially relevant studies.

Supplemental Table S3 Confidence result of identified eligible SRs and MAs.

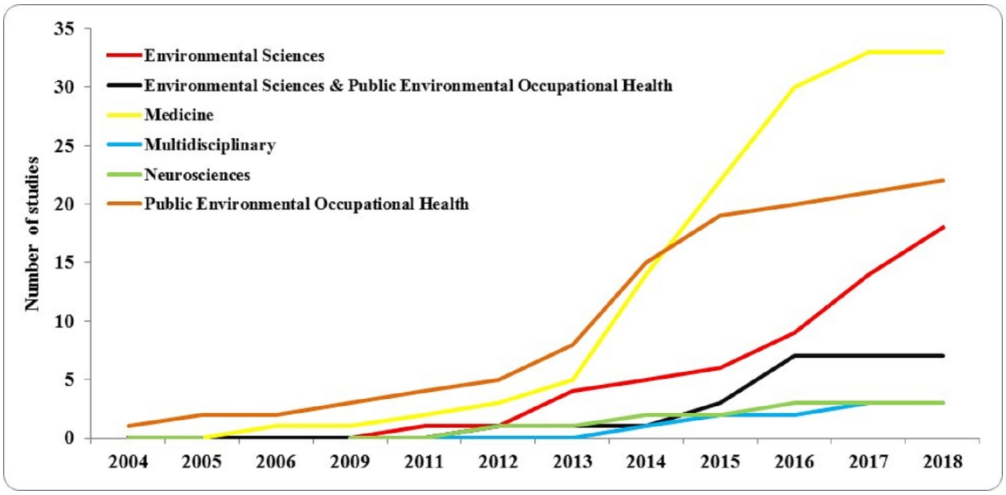
The list includes outdoor air pollution categories, health outcomes categories and the confidence result based on SURE.



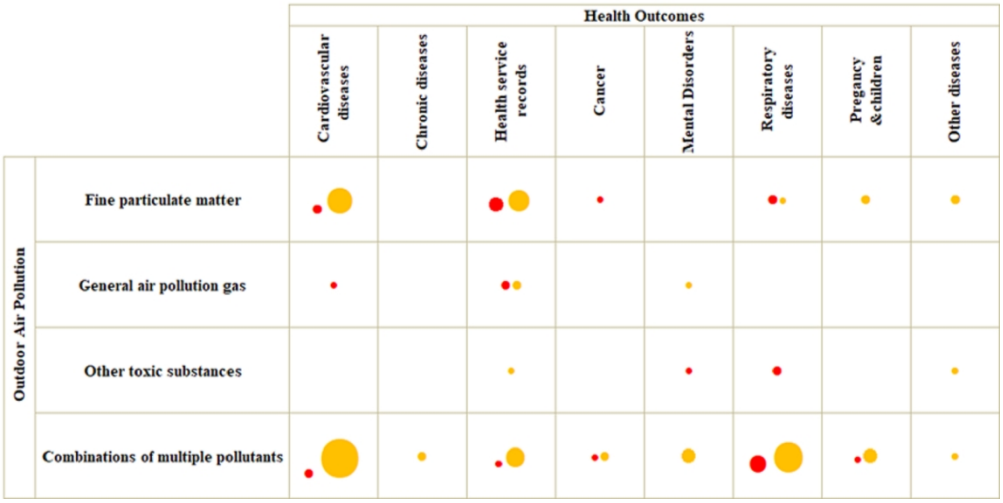
Systematic literatures search process for eligible SRs and MAs. SRs, systematic reviews; MAs, meta analyses.



Regions and countries distribution of eligible SRs and MAs. The data of regions and countries are based on the information of corresponding authors. SRs, systematic reviews; MAs, meta analyses.



Numbers of inclusive eligible SRs and MAs in six research fields between 2004 and 2018. The number of the eligible SRs and MAs saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years. SRs, systematic reviews; MAs, meta analyses.



EGM for health outcomes affected by outdoor air pollution. The colors of bubble represent the confidence of included SRs and MAs, red color represents low confidence and yellow color represents medium confidence. The sizes of bubble indicate the relative number of included SRs and MAs, and a larger bubble represents a larger study sample size in each grid. SRs, systematic reviews; MAs, meta analyses.

Supplemental Table S1:

List of outdoor air pollution and health outcome related terms.

Concept	Type	Detail
Outdoor air pollution	General air pollution gas	Ozone(O_3), sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen dioxide (NO_2)
	Fine particulate matter	Total suspended particle, suspended particulate matter, $PM_{2.5}$, PM_{10}
	Other toxic substances	Toxic air pollutants, volatile organic pollutants, nitrogen oxides (NO_x)
Health outcomes	Respiratory diseases	Asthma, lung cancer, respiratory infections, respiratory disorder
	Chronic diseases	Diabetes, chronic obstructive pulmonary disease
	Cardiovascular diseases	Hypertension, heart rate variability, heart attack, cardiopulmonary disease, ischemic heart disease, blood coagulation, deep vein thrombosis, stroke
	Health records	Morbidity, hospital admissions, outpatient visits, ER visits and mortality
	Other diseases	DNA methylation changes, neurobehavioral functions, inflammatory disease, skin disease, abortion, Alzheimer's disease, disability, cognitive function, Parkinson's disease

O_3, Ozone; SO_2, sulfur dioxide; CO, carbon monoxide; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; ER, emergence room.

Supplemental Table S2 [a]:

Search strategies for the potentially relevant studies.

1. Database and time period

PubMed Clinical Queries Database – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	Search ((((((((((Ozone*[MeSH Terms]) OR sulfur dioxide*[MeSH Terms]) OR carbon monoxide*[MeSH Terms]) OR nitrogen dioxide*[MeSH Terms]) OR PM2.5[MeSH Terms]) OR PM10[MeSH Terms]) OR total suspended particle*[MeSH Terms]) OR suspended particulate matter*[MeSH Terms]) OR Toxic air pollutant*[MeSH Terms]) OR volatile organic pollutant*[MeSH Terms]) OR nitrogen oxide*[MeSH Terms]	138,175
#2	Search ((((((((((((((((((((((((((asthma[MeSH Terms]) OR lung cancer[MeSH Terms]) OR respiratory infection*[MeSH Terms]) OR respiratory disorder*[MeSH Terms]) OR diabetes[MeSH Terms]) OR chronic respiratory disease*[MeSH Terms]) OR chronic obstructive pulmonary disease*[MeSH Terms]) OR hypertension[MeSH Terms]) OR heart rate variability[MeSH Terms]) OR heart attack[MeSH Terms]) OR cardiopulmonary disease*[MeSH Terms]) OR ischemic heart disease*[MeSH Terms]) OR blood coagulation*[MeSH Terms]) OR deep vein thrombosis[MeSH Terms]) OR stroke[MeSH Terms]) OR morbidity[MeSH Terms]) OR hospital admission*[MeSH Terms]) OR outpatient visit*[MeSH Terms]) OR emergency room visit*[MeSH Terms]) OR mortality[MeSH Terms]) OR DNA methylation change*[MeSH Terms]) OR neurobehavioral function[MeSH Terms]) OR Inflammatory disease*[MeSH Terms]) OR skin disease*[MeSH Terms]) OR abortion[MeSH Terms]) OR Alzheimer's disease*[MeSH Terms]) OR	3,125,123

item	Search input	result
	disability[MeSH Terms]) OR cognitive function[MeSH Terms]) OR Parkinson's disease*[MeSH Terms]	
#3	Search (outdoor[Text Word]) AND air pollution[Text Word]	3,132
#4	meta analysis[Title/Abstract]	111,455
	#1 AND #2 AND #3 AND #4	0
	#3 AND #4	**44**
#5	systematic review[Title/Abstract]	111,428
	#1 AND #2 AND #3 AND #5	0
	#3 AND #5	**38**

After duplication: 59

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1. Database and time period

Scopus – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	TITLE-ABS-KEY ("Ozone*") OR TITLE-ABS-KEY ("sulfur dioxide*") OR TITLE-ABS-KEY ("carbon monoxide*") OR TITLE-ABS-KEY ("nitrogen dioxide*") OR TITLE-ABS-KEY (pm2.5) OR TITLE-ABS-KEY (pm10) OR TITLE-ABS-KEY (total AND suspended AND particle*) OR TITLE-ABS-KEY (suspended AND particulate AND matter*) OR TITLE-ABS-KEY (toxic AND air AND pollutant*) OR TITLE-ABS-KEY ("volatile organic pollutant*") OR TITLE-ABS-KEY ("nitrogen oxide*")	327,759
#2	TITLE-ABS-KEY ("asthma") OR TITLE-ABS-KEY ("lung cancer") OR TITLE-ABS-KEY ("respiratory infection*") OR TITLE-ABS-KEY ("respiratory disorder*") OR TITLE-ABS-KEY ("diabetes*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("hypertension") OR TITLE-ABS-KEY ("heart rate variability") OR TITLE-	4,445,123

item	Search input	result
	ABS-KEY ("heart attack") OR TITLE-ABS-KEY ("cardiopulmonary disease*") OR TITLE-ABS-KEY ("ischemic heart disease*") OR TITLE-ABS-KEY ("blood coagulation") OR TITLE-ABS-KEY ("deep vein thrombosis") OR TITLE-ABS-KEY (stroke) OR TITLE-ABS-KEY (morbidity) OR TITLE-ABS-KEY (" hospital admission*") OR TITLE-ABS-KEY ("outpatient visit*") OR TITLE-ABS-KEY (" emergency room visit*") OR TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (" DNA Methylation Change*") OR TITLE-ABS-KEY ("neurobehavioral function*") OR TITLE-ABS-KEY (" Inflammatory disease* ") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (abortion) OR TITLE-ABS-KEY ("Alzheimer's disease*") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (disability) OR TITLE-ABS-KEY ("cognitive function") OR TITLE-ABS-KEY ("Parkinson's disease*")	
#3	ALL (outdoor) AND ALL (" air pollution*")	31,240
#4	TITLE-ABS-KEY ("meta analysis*") OR TITLE-ABS-KEY ("systematic review*")	330,816
	#1 AND #2 AND #3 AND #4	**216**

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1. Database and time period

Web of science– inception-6/24/2018

2. Language:

English

3. Search strategy:

item	search	result
#1	TS = (Ozone* OR sulfur dioxide* OR carbon monoxide* OR nitrogen dioxide* OR PM2.5 OR PM10 OR total suspended particle* OR suspended particulate matter* OR Toxic air pollutant* OR volatile organic pollutant OR nitrogen oxide*)	674,294

item	search	result
#2	TS = (asthma OR lung cancer OR respiratory infection* OR respiratory disorder* OR diabetes OR chronic respiratory disease* OR chronic obstructive pulmonary disease* OR hypertension OR heart rate variability OR heart attack OR cardiopulmonary disease* OR ischemic heart disease* OR blood coagulation* OR deep vein thrombosis OR stroke OR morbidity OR hospital admission* OR outpatient visit* OR emergency room visit* OR mortality OR DNA methylation change* OR neurobehavioral function OR Inflammatory disease* OR skin disease* OR abortion OR Alzheimer's disease* OR disability OR cognitive function OR Parkinson's disease*)	7,157,410
#3	TS = (outdoor AND air pollution*)	10,814
#4	TS = ("meta analysis ")	174,699
	#1 AND #2 AND #3 AND #4	**53**
#5	TS = ("systematic review ")	163,736
	#1 AND #2 AND #3 AND #5	**33**

[a]: Database Cochrane search result was zero.

Supplemental Table S3:
Confidence result of identified eligible SRs and MAs.

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yang et al (2018)[1]	Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Zhao et al (2018)[2]	Ambient ozone exposure and mental health: A systematic review of epidemiological studies	Germany	General air pollution gas	Mental disorders	Medium
Newell et al (2018)[3]	Cardiorespiratory health effects of gaseous ambient air pollution exposure in low and middle income countries: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Health Records	Medium
An et al (2018)[4]	Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis	America	Mixed air pollution	Other diseases	Medium
Zhang, Wang & Lu (2018)[5]	Exposure to nitrogen dioxide and chronic obstructive pulmonary disease (COPD) in adults: a systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
DeVries, Kriebel & Sama (2017)[6]	Outdoor Air Pollution and COPD-Related Emergency Department Visits, Hospital Admissions, and Mortality: A Meta-Analysis	America	Mixed air pollution	Health Records	Medium
Khreis et al (2017)[7]	Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Fajersztajn et al (2017)[8]	Short-term effects of fine particulate matter pollution on daily health events in Latin America: a systematic review and meta-analysis	Brazil	Fine particulate matter	Health Records	Medium
Huang et al (2017)[9]	Relationship between exposure to PM2.5 and lung cancer incidence and mortality: A meta-analysis	China	Fine particulate matter	Health Records	Medium
Nguyen Thi Trang et al (2017)[10]	Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-series and case-crossover studies	Switzerland	Mixed air pollution	Respiratory diseases	Medium
Orellano et al (2017)[11]	Effect of outdoor air pollution on asthma exacerbations in children and adults: Systematic review and multilevel meta-analysis	Argentina	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Zhao et al (2017)[12]	The impact of short-term exposure to air pollutants on the onset of out-of-hospital cardiac arrest: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Achilleos et al (2017)[13]	Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis	America	Fine particulate matter	Health Records	Low
Ngoc et al (2017)[14]	Systematic review and meta-analysis of human skin diseases due to particulate matter	South Korea	Fine particulate matter	Other diseases	Medium
Lin et al (2017)[15]	Lung cancer mortality of residents living near petrochemical industrial complexes: a meta-analysis	China	Other toxic substances	Health Records	Medium
Froes Asmus et al (2016)[16]	A Systematic Review of Children's Environmental Health in Brazil	Brazil	Mixed air pollution	Respiratory diseases	Low
Zhang et al (2016b)[17]	Association between atmospheric particulate matter and adverse pregnancy outcomes in the population	China	Fine particulate matter	Pregnancy & children	Medium
Lim et al (2016)[18]	Short-term effect of fine particulate matter on children's hospital admissions and emergency department visits for asthma: A systematic review and meta-analysis	South Korea	Fine particulate matter	Respiratory diseases	Medium
Mills et al (2016)[19]	Distinguishing the associations between daily mortality and hospital admissions and nitrogen dioxide from those of particulate matter: A systematic review and meta-analysis	United Kingdom	General air pollution gas	Health Records	Medium
Fan et al (2016)[20]	The impact of PM2.5 on asthma emergency department visits: a systematic review and meta-analysis	China	Fine particulate matter	Health Records	Medium
Bloemsma, Hoek & Smit, 2016)[21]	Panel studies of air pollution in patients with COPD: Systematic review and meta-analysis	Netherlands	Fine particulate matter	Cardiovascular diseases	Medium
Li et al (2016)[22]	Major air pollutants and risk of COPD exacerbations: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Franchini et al (2016)[23]	Association between particulate air pollution and venous thromboembolism: A systematic literature review	Italy	Fine particulate matter	Cardiovascular diseases	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Pascal et al (2016)[24]	The mortality impacts of fine particles in France	France	Fine particulate matter	Health Records	Medium
Checa Vizcaino et al (2016)[25]	Outdoor air pollution and human infertility: a systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Power et al (2016)[26]	Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research	America	Mixed air pollution	Mental disorders	Medium
Song et al (2016)[27]	Short-term exposure to air pollution and cardiac arrhythmia: A meta-analysis and systematic review	China	Mixed air pollution	Cardiovascular diseases	Medium
Flores-Pajot et al (2016)[28]	Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: A review and meta-analysis	Canada	Mixed air pollution	Mental disorders	Medium
Hou et al (2016)[29]	The role of the PM2.5-associated metals in pathogenesis of child Mycoplasma Pneumoniae infections: a systematic review	China	Fine particulate matter	Respiratory diseases	Low
Zhang et al (2016a)[30]	Short-term exposure to air pollution and morbidity of COPD and asthma in East Asian area: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2016)[31]	Impact of air quality guidelines on COPD sufferers	America	Mixed air pollution	Cardiovascular diseases	Medium
Cai et al (2016)[32]	Associations of Short-Term and Long-Term Exposure to Ambient Air Pollutants With Hypertension: A Systematic Review and Meta-Analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Luo et al (2015)[33]	Short-term exposure to particulate air pollution and risk of myocardial infarction: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2015)[34]	Fine particle components and health - A systematic review and meta-analysis of epidemiological time series studies of daily mortality and hospital admissions	United Kingdom	Mixed air pollution	Health Records	Low
Hamra et al (2015)[35]	Lung cancer and exposure to nitrogen dioxide and traffic: A systematic review and meta-analysis	America	Mixed air pollution	Cancer	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Chen et al (2015)[36]	Traffic-related air pollution and lung cancer: A meta-analysis	China	Mixed air pollution	Cancer	Medium
Jadambaa et al (2015)[37]	The impact of the environment on health in Mongolia: A systematic review	Mongolia	Mixed air pollution	Respiratory diseases	Low
Eze et al (2015)[38]	Association between ambient air pollution and diabetes mellitus in Europe and North America: Systematic review and meta-analysis	Switzerland	Mixed air pollution	Chronic diseases	Medium
Nurmatov et al (2015)[39]	Volatile organic compounds and risk of asthma and allergy: A systematic review	United Kingdom	Other toxic substances	Respiratory diseases	Low
Cui et al (2015)[40]	Ambient particulate matter and lung cancer incidence and mortality: A meta-analysis of prospective studies	China	Fine particulate matter	Health Records	Medium
Rodriguez-Villamizar et al (2015)[41]	The effects of outdoor air pollution on the respiratory health of Canadian children: A systematic review of epidemiological studies	Canada	Mixed air pollution	Respiratory diseases	Low
Bowatte et al (2015)[42]	The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: A systematic review and a meta-analysis of birth cohort studies	Australia	Mixed air pollution	Respiratory diseases	Medium
Shah et al (2015)[43]	Short term exposure to air pollution and stroke: Systematic review and meta-analysis	United Kingdom	Mixed air pollution	Cardiovascular diseases	Medium
Scheers et al (2015)[44]	Long-Term Exposure to Particulate Matter Air Pollution Is a Risk Factor for Stroke: Meta-Analytical Evidence	Belgium	Fine particulate matter	Cardiovascular diseases	Medium
Filippini et al (2015)[45]	A review and meta-analysis of outdoor air pollution and risk of childhood leukemia	Italy	Mixed air pollution	Cardiovascular diseases	Low
Frutos et al (2015)[46]	Impact of air pollution on fertility: A systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Zheng et al (2015)[47]	Association between Air pollutants and asthma emergency room visits and hospital admissions in time series studies: A systematic review and meta-Analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2015)[48]	Association of exposure to particular matter and carotid intima-media thickness: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Balti et al (2014)[49]	Air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis	South Africa	Mixed air pollution	Chronic diseases	Medium
Faustini, Rapp & Forastiere (2014)[50]	Nitrogen dioxide and mortality: Review and meta-analysis of long-term studies	Italy	Mixed air pollution	Health Records	Medium
Li et al (2014)[51]	Mechanisms in endocrinology: Main air pollutants and diabetes-associated mortality: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Rossignol, Genuis & Frye (2014)[52]	Environmental toxicants and autism spectrum disorders: A systematic review	America	Other toxic substances	Mental disorders	Low
Hamra et al (2014)[53]	Outdoor particulate matter exposure and lung cancer: A systematic review and meta-analysis	France	Fine particulate matter	Cancer	Low
Hu et al (2014)[54]	Ambient air pollution and hypertensive disorders of pregnancy: A systematic review and meta-analysis	America	Mixed air pollution	Cardiovascular diseases	Medium
Pedersen et al (2014)[55]	Ambient air pollution and pregnancy-induced hypertensive disorders: A systematic review and meta-analysis	Spain	Mixed air pollution	Cardiovascular diseases	Medium
Bell, Zanobetti & Dominici (2014)[56]	Who is more affected by ozone pollution? A systematic review and meta-analysis	America	General air pollution gas	Health Records	Low
Shin et al (2014)[57]	Outdoor fine particles and nonfatal strokes: Systematic review and meta-analysis	America	Fine particulate matter	Cardiovascular diseases	Low
Song et al (2014)[58]	The global contribution of outdoor air pollution to the incidence, prevalence, mortality and hospital admission for chronic obstructive pulmonary disease: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2014)[59]	Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: A systematic review and meta-analysis	United Kingdom	Fine particulate matter	Health Records	Low
Dick et al (2014b)[60]	A systematic review of associations between environmental exposures and development of asthma in children aged up to 9 years	United Kingdom	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yamamoto, Phalkey & Malik (2014)[61]	A systematic review of air pollution as a risk factor for cardiovascular disease in South Asia: Limited evidence from India and Pakistan	Germany	Mixed air pollution	Cardiovascular diseases	Medium
Chen et al (2014)[62]	Effects of air pollution on the risk of congenital anomalies: A systematic review and meta-analysis	France	Mixed air pollution	Mental disorders	Medium
Dick et al (2014a)[63]	Associations between environmental exposures and asthma control and exacerbations in young children: A systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Teng et al (2014)[64]	A systematic review of air pollution and incidence of out-of-hospital cardiac arrest	Australia	Mixed air pollution	Cardiovascular diseases	Low
Vawda et al (2014)[65]	Associations between inflammatory and immune response genes and adverse respiratory outcomes following exposure to outdoor air pollution: A huge systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Low
Yu et al (2014)[66]	Short-term effects of particulate matter on stroke attack: Meta-regression and meta-analyses	China	Fine particulate matter	Cardiovascular diseases	Medium
Liang et al (2014)[67]	Effect of exposure to PM2.5 on blood pressure: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Zhu et al (2013)[68]	The relationship between particulate matter (PM10) and hospitalizations and mortality of chronic obstructive pulmonary disease: A meta-analysis	China	Fine particulate matter	Health Records	Low
Hoek et al (2013)[69]	Long-term air pollution exposure and cardio-respiratory mortality: A review	Netherlands	Fine particulate matter	Health Records	Medium
Anderson, Favarato & Atkinson (2013a)[70]	Long-term exposure to outdoor air pollution and the prevalence of asthma: Meta-analysis of multi-community prevalence studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Anderson, Favarato & Atkinson (2013b)[71]	Long-term exposure to air pollution and the incidence of asthma: Meta-analysis of cohort studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Bell, Zanobetti & Dominici (2013)[72]	Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis.	America	Fine particulate matter	Other diseases	Medium
Nieuwenhuijsen et al (2013)[73]	Environmental risk factors of pregnancy outcomes: a summary of recent meta-analyses of epidemiological studies.	Spain	Fine particulate matter	Pregnancy & children	Medium
Mehta et al (2013)[74]	Ambient particulate air pollution and acute lower respiratory infections: A systematic review and implications for estimating the global burden of disease	America	Mixed air pollution	Respiratory diseases	Medium
Park, Bae & Hong (2013)[75]	PM10 exposure and non-accidental mortality in Asian populations: A meta-analysis of time-series and case-crossover studies	South Korea	Fine particulate matter	Health Records	Medium
Stieb et al (2012)[76]	Ambient air pollution, birth weight and preterm birth: A systematic review and meta-analysis	Canada	Mixed air pollution	Pregnancy & children	Medium
Gasana et al (2012)[77]	Motor vehicle air pollution and asthma in children: A meta-analysis	America	Mixed air pollution	Respiratory diseases	Medium
Li et al (2012)[78]	Meta-Analysis of Association between Particulate Matter and Stroke Attack	China	Fine particulate matter	Cardiovascular diseases	Medium
Takenoue et al (2012)[79]	Influence of outdoor NO2 exposure on asthma in childhood: Meta-analysis	Japan	General air pollution gas	Health Records	Medium
Tashakkor, Chow & Carlsten, 2011)[80]	Modification by antioxidant supplementation of changes in human lung function associated with air pollutant exposure: A systematic review	Canada	Other toxic substances	Respiratory diseases	Low
Afshari et al (2011)[81]	Inhaled nitric oxide for acute respiratory distress syndrome and acute lung injury in adults and children: A systematic review with meta-analysis and trial sequential analysis	Denmark	Other toxic substances	Other diseases	Medium
Shah, Balkhair & Knowledge Synth Grp Determinants (2011)[82]	Air pollution and birth outcomes: A systematic review	Canada	Mixed air pollution	Pregnancy & children	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Forbes et al (2009)[83]	Chronic exposure to outdoor air pollution and diagnosed cardiovascular disease: meta-analysis of three large cross-sectional surveys.	United Kingdom	General air pollution gas	Cardiovascular diseases	Low
Mahjub & Gh (2006)[84]	Meta-analysis of case-referent studies of specific environmental or occupational pollutants on lung cancer	Iran	Mixed air pollution	Cancer	Medium
Ito, De Leon & Lippmann (2005)[85]	Associations between ozone and daily mortality: Analysis and meta-analysis	America	General air pollution gas	Health Records	Low
Ward & Ayres (2004)[86]	Particulate air pollution and panel studies in children: a systematic review.	United Kingdom	Fine particulate matter	Respiratory diseases	Low

SRs, systematic reviews; MAs, meta analyses.

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BMJ Open

Exposure to outdoor air pollution and its human-related health outcomes: an evidence gap map

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031312.R2
Article Type:	Original research
Date Submitted by the Author:	18-Nov-2019
Complete List of Authors:	sun, zhuanlan; Tongji University, Zhu, Demi; Shanghai Jiaotong University
Primary Subject Heading:	Health policy
Secondary Subject Heading:	Health policy
Keywords:	outdoor air pollution, health outcomes, evidence gap map

Exposure to outdoor air pollution and its human-related health outcomes: an evidence gap map

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ABSTRACT

Objectives Outdoor air pollution is a serious environmental problem worldwide. Current systematic reviews (SRs) and meta analyses (MAs) mostly focused on some specific health outcomes or some specific air pollution.

Design This evidence gap map (EGM) is to identify existing gaps from SRs and MAs and report them in broad topic areas.

Data Sources PubMed, Cochrane, Scopus and Web of Science were searched from their inception until June 2018. Citations and reference lists were traced.

Eligibility Criteria SRs and MAs that investigated the impact of outdoor air pollution on human health outcomes were collected. This study excluded original articles and qualitative review articles.

Data extraction and synthesis Characteristics of the included SRs and MAs were extracted and summarised. Extracted data included authors, publication year, location of the corresponding author(s), publication journal discipline, study design, study duration, sample size, study region, target population, types of air pollution and health outcomes.

Results Asia and North America published 93% of SRs and MAs included in this EGM. 31% of the SRs and MAs (27/86) included primary studies conducted in 5-10 countries. Publication trends of them are increasing in the recent 10 years. A total of 2,864 primary studies were included. The median number of included primary studies was 20 (range, 7-167). Cohort studies, case-crossover studies and time-series studies were the top 3 mostly used study designs. The mostly researched population was the group of all ages (46/86, 53%). Cardiovascular diseases, respiratory diseases and health service records were mostly reported. Lacking of definite diagnostic criteria, unclearly reporting of air pollution exposure and time period of primary studies were the main research gaps.

Conclusions This EGM provided a visual overview of health outcomes affected by outdoor air pollution exposure. Future research should focus on chronic diseases, cancer and mental disorders.

Strengths and limitations of this study

This study established an evidence gap map, as a two-dimensional matrix, of outdoor air pollution and health outcomes, the row and column of the array included all categories of outdoor air pollution and human-related health outcomes respectively.

This evidence gap map focused on a broad range of air pollution and human health outcomes based on a systematic search of four databases from their inception until June 2018.

The bubble plot was used to visualize the evidence gap, the colour represented the confidence of included systematic reviews and the size indicated the number of included systematic reviews.

Only systematic reviews and meta analyses were included in this evidence gap map.

The publication language of included systematic reviews and meta analyses was restricted in English, thus possibly missing pertinent information written in other languages.

INTRODUCTION

Outdoor air pollution is a serious environmental problem and a major public health concern worldwide, which has caused approximately 4.2 million global deaths in 2016.[1] It is a severe invisible killer posing serious human health hazards, especially in developing countries, which industrialization and urbanization are speeding up.[2] There are many common types of air pollutants, such as fine particulate matter ($PM_{2.5}$ and PM_{10}), ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_2 and NO_x), volatile organic pollutants and some other toxic air pollutants. The human-related health outcomes affected by such air pollutants have been studied for decades. Researchers from various disciplines all over the world have shown constant interest in the health effects of outdoor air pollution, such as cardiovascular disease, respiratory disease, cancer, Alzheimer's disease and so on.[3–6]

Systematic reviews (SRs) aim to synthesis all relevant high-quality evidence on a specific topic in terms of the health outcomes of outdoor air pollution.[7] It was reported that outdoor NO_2 exposure triggered asthma,[8,9] other studies identified human mortality was positively associated with $PM_{2.5}$ exposure.[10,11] However, many studies focused on interactive effects with regard to several types of health outcomes affected by various air pollutants,[12,13] and there are some overlapping SRs implied inconsistent results.[14,15] The specific topic of SRs findings on particular factors cannot be used to provide a comprehensive overview of air pollution related health outcomes.

To overcome this barrier, some novel knowledge synthesis approaches (e.g., scoping review, systematic mapping, evidence mapping, etc.) have been developed to evaluate the overall effects of evidence on a broader area, highlighting both current knowledge and gaps in evidence.[16–19] Evidence gap map (EGM), an emerging evidence synthesis method, was proposed to systematically and comprehensively assess intervention effects and outcomes in a user-friendly two-dimensional matrix framework. It can also efficiently visualize the existing evidence in a map with a critical quality appraisal for policy and research implications.[20,21]

EGM can inform a strategic approach to build the evidence based on particular issues. Water, sanitation and hygiene interventions were evaluated by 3ie to inform policy decisions and address the evidence gap.[21] 3ie, known as the International Initiative for Impact Evaluation, is a global collaboration focus on evidence synthesis. To our knowledge, there are little research overviewed the outdoor air pollution exposure related health outcomes by using EGM.

We constructed an EGM on the health effects of outdoor air pollution by comprehensively summarising existing SRs and meta-analyses (MAs). The main purpose of this EGM was to identify the evidence gaps for potential research prioritization. In addition, it also can be used in the evidence-based environmental policy making support.

MATERIALS & METHODS

EGM is a newly developed method of knowledge synthesis, which is similar to evidence mapping.[18] There is no standard methodology guideline available for evidence mapping

currently.[22] We followed the methodology framework presented by Snilstveit et al to conduct this EGM.[21] Establishing the framework was divided into six steps: developing scope; setting inclusive criteria; searching relevant studies; selecting studies; extracting data and appraising quality; summarising results.

Scope development

The established framework was a two-dimensional matrix of outdoor air pollution and health outcomes. It derived from the major policies of interest and existing academic literature. The row and column of the array included all categories of outdoor air pollution and human-related health outcomes respectively.

To improve the quality of EGM, stakeholders, including academic researchers, policymakers, practitioners and funders, were recruited. The academic researchers are from environmental science, public health, epidemiology and economics. Some researchers have interdisciplinary research experience. The policymakers, funders and practitioners are from environmental protection administrations and public health administrations. A consultation with key stakeholders was conducted to ensure the acceptance of the research framework. It was carried out at the process of study inclusion, literature search and data extraction. All the key stakeholders were invited to take part in the consultation to determine the scope and the technologies of the EGM.

Study inclusion criteria

Following 3ie's guideline, we included systematic review and meta-analysis studies, and summarised all the available evidence on human-related health outcomes affected by particular air pollution.[23]

Study search

Four electronic databases, PubMed, Cochrane, Scopus and Web of Science, were searched from their inception until June 2018. The language was restricted to English. We compiled a list of outdoor air pollution and health outcome terms by reviewing the potential text words in the titles or abstracts of the most pertinent literature (supplemental table s1), this process was conducted by consulting with experts who are members of the Committee on Public Health and Urban Environment Management in China. We then used advanced database search strategies on key words, combined with Boolean operators (AND, OR, NOT) and wild card symbols (*), so as to search for the potentially relevant literature (supplemental table s2). This study focused on the health outcomes affected by outdoor air pollution, thus, the term "air pollution" which contains some contaminants inside private and public buildings was not included in the search strategy. To prevent any relevant literature from missing, we subsequently traced citations and reference lists of literature to generate more relevant systematic review and meta-analysis studies.

Inclusion assessment

Table 1 Inclusion and exclusion criteria used in this EGM for eligible studies

Inclusive criteria	Exclusive criteria
Studies types	**Studies type**
SRs and MAs	Indoor air pollution
Studies methods	Primary studies
Quantitative SRs	**Studies methods**
Studies conclusion	Qualitative reviews only
Data supported outcome relevant to outdoor air pollution	

SRs, systematic reviews; MAs, meta-analyses.

The first step of inclusion assessment involved screening the titles and abstracts of SRs and MAs by two reviewers independently. The inclusion and exclusion criteria for EGM were discussed by the team members at the beginning of this process (table 1). Primary studies, such as observational studies, time-series studies and causal inference studies, were not included. The definition of outdoor air pollution is that exposure takes place outside of the built environment. Both the health outcomes and outdoor air pollution reported in the SRs and MAs are eligible. Reference management software Mendeley was used to systematically remove duplicated literature and assess potential literature that meets the inclusion criteria.

The second step of the study selection stage was the full-text retrieve of all potentially eligible articles, which was independently screened by the two reviewers as well. If disagreements occurred between them, a third specialist made the final decision.

Data extraction and critical appraisal

Characteristics of the included SRs and MAs were extracted and summarised by one reviewer and checked for accuracy by the other. Extracted data included authors, publication year, location of the corresponding author(s), publication journal discipline, study design, study duration, sample size, study region, target population, types of air pollution and health outcomes (table 2). Other categories, such as key results, would extract based on the advice of some researchers from public health and policymakers. We categorized the results of health outcomes into three parts: positive, negative and ambiguous. Positive represents air pollution has harmful effects on human health outcomes. Negative means no harmful effect was found in the MAs. Air pollution was categorized as general air pollution gas, fine particulate matter, other toxic substances and combinations of multiple pollutants. The definition of "combinations of multiple pollutants" is the mixture of two or more air pollutants as followings: O_3, SO_2, CO, NO_2, $PM_{2.5}$, PM_{10}, suspended particulate matter and total suspended particle.

Table 2 Information to be collected during the data extraction stage

Study design	Study population	Exposures	Outcome information
Author(s)	Sample size	Types of air pollution	Health outcomes
Publication Year	Study region		Key results
Location of the corresponding author(s)	Target population		
Publication journal discipline			
Study design			
Study duration			

a: The discipline catalog is from the Journal Citation Report published by Web of Science.

The potential study designs and the inherent characteristics (strengths and limitations) of each design make the quality assessment complex.[24] We applied the Supporting the Use for Research Evidence (SURE) checklist to appraise the quality of included SRs and MAs in terms of the confidence, [21] rating them as high, medium or low confidence.[20] SURE is a mechanism aims to strengthen the evidence-informed policymaking, which is more appropriate for our research. The SURE checklist was designed to assess three dimensions of the included SRs and MAs: (1) methods used to identify, include and critically appraise studies, (2) methods used to analyze the findings and (3) overall assessment of the reliability of the review. Two authors independently assessed the quality of the included SRs and MAs. Any difference would be resolved by consulting with a third researcher.

Summarization and visualization

To provide a snapshot of what is known and the areas where evidence is lacking, a bubble plot was used to represent the extent of health outcomes affected by outdoor air pollution. We followed the visual representation of 3ie's two-dimensional framework to generate the bubble plot. [21] In the EGM plot, traffic light colour indicates three levels of findings' confidence, which assessed by using the SURE checklist. Red bubbles represent low confidence, yellow ones represent medium, and green ones represent high confidence. Bubble size represents the quantity of corresponding SRs and MAs.

Patient and public involvement

No patients or public involved in this EGM.

RESULTS

Figure 1 displays the systematic literature search process for EGM. A literature search of four electronic databases yielded 361 potentially relevant studies. After removing duplicate research, 266 studies were collected. Based on screening the titles and the abstracts, 118 SRs and MAs were assessed as being relevant to the EGM. To avoid missing potential studies, we also manually searched the relevant studies in the top five impact factor periodicals, which were chosen in the collection of our included published SRs and MAs. Tracing of citations and reference lists made that 5 more relevant studies were included at the end of this process. In total, 123 SRs and MAs were included in the full-text screening analysis. Finally, 86 eligible articles were included in our EGM. In all 86 SRs and MAs, a total of 2,864 original studies were included. The median number of original studies was 20 (range, 7-167), the variance value of which was 31.99.

General descriptions summary of included SRs and MAs

Of the 86 included SRs and MAs, most of them were published in Europe, Asia and North America, with the proportion of 37%, 34% and 22% respectively (table 3). As illustrates in figure 2, SRs and MAs published in the top three continents were concentrated in a small group of

countries, with China, the USA and the UK on the top of the list. Little evidence came from Africa, Australia and South America, with an overall proportion of only 6%. The distribution of publications was unbalanced.

The population of included SRs and MAs were categorized into seven subgroups: infants, children and adolescents, adults, women and pregnancy, all ages, elderly and not specified (table 3). The largest population affected by outdoor air pollution fell under the group of all ages (46/86; 53%), followed by the group of children and adolescents under the age of 20, with a percentage of 17% (15/86). The infants and elderly groups shared only 2%, however, these two groups of people were mostly affected by air pollution.

Almost half of the available primary studies included in SRs and MAs were conducted in more than 5 countries. 21% of the SRs and MAs only included primary studies conducted in less than 5 countries. The sample size of the primary studies included in the SRs and MAs varied with a wide range, the number of which ranged from less than one hundred to millions (range: 83-11,850,884 participants).

Table 3 General descriptions for included SRs and MAs

(n=86)	N	%		N	%
Continent [a]			**Numbers of original study**		
Africa	1	1%	<10 studies	10	12%
Australia	2	2%	10~30 studies	46	53%
South America	3	3%	30~60 studies	13	15%
North America	19	22%	>60 studies	13	15%
Asia	29	34%	Not clearly mentioned	4	5%
Europe	32	37%	**Study period**		
Countries of primary studies included in SRs and MAs			<10 years	11	13%
<5 countries	18	21%	10 ~ 20 years	23	27%
5 ~ 10 countries	27	31%	> 20 years	7	8%
10 ~ 20 countries	15	17%	Not clearly mentioned	45	52%
> 20 countries	1	1%	**Types of study design**		
Not clearly mentioned [b]	25	29%	Single	13	15%
Population			Multiply	73	85%
Infants	2	2%	**Study design**		
Children & Adolescents	15	17%	Cohort	41	
Adults	7	8%	Case-crossover	27	
Elderly	2	2%	Time-series	25	
Women & Pregnancy	4	5%	Case-control	24	
All ages	46	53%	Cross-sectional	20	
Not specified	10	12%	**Sample size(range)**	(83-11,850,884)	

SRs and MAs, systematic reviews and meta-analyses.

Of the study design, 15% (13/86) of the included SRs and MAs were conducted by using a single study design, the rest 73 SRs and MAs originated from primary studies with multiple study designs. The top five mostly used study designs of the primary studies included in the SRs and MAs were cohort, case-crossover, time-series, case-control and cross-sectional, the

corresponding number was 41, 27, 25, 24 and 20 respectively. The time period, which means the publication date intervals of primary studies included in the SRs and MAs, were mostly (51%) unclearly reported.

Publication trends of included SRs and MAs

The included SRs and MAs were mainly conducted in six research fields. As the cumulative frequency trend chart displays in figure 3, the number of SRs showed an increasing trend from 2004 to 2018. Most of the included SRs and MAs were published in the recent six years, with no SRs published before the year 2004. All included SRs and MAs were categorized by using the Journal Citation Report in Web of Science database. There was an increasing trend in the number of publications in the fields of medicine and public environmental occupational health from 2004 to 2013, and the trend remarkably raised from 2013 till now, especially in medical research. The environmental sciences saw a rising trend since 2011, then the trend spiked up in the years 2012 and 2015 respectively, and reached its peak number in 2017. Three disciplines, including environmental sciences and public environmental occupational health, multidisciplinary and neurosciences, increased smoothly since the year 2011.

Summary by health outcome groups

We categorized health outcomes into eight groups based on the specialists' suggestions: cardiovascular diseases, chronic diseases, health service records, cancer, mental disorders, respiratory diseases, pregnancy and children and other diseases, which were important features of the EGM visualization. The categorized list of health outcomes is shown in table 4.

Table 4 The categorized list of health outcomes

Health outcome groups	Health outcome of inclusive studies
Respiratory diseases	Asthma, respiratory diseases, ALRI
Chronic diseases	Diabetes
Cardiovascular diseases	Hypertension, BP, COPD, OHCA, VTE, CVD, myocardial infarction, Arrhythmia, stroke
Health service records	Morbidity, hospital admissions, ED visits, mortality
Cancer	Lung cancer
Pregnancy & Children	Fertility, pregnancy, Birth
Mental disorders	Mental health, cognition, ASD
Other diseases	Physical inactivity, skin disease, health risks

ALRI, acute lower respiratory infections; BP, blood pressure; COPD, chronic obstructive pulmonary disease; OHCA, out-of-hospital cardiac arrest; VTE, venous thromboembolism; CVD, cardiovascular diseases; ED, emergency department; ASD, autism spectrum disorder.

The inclusive studies in our EGM were summarised based on health outcome groups (table 5). The information about the types of air pollution, the number of primary studies, population groups, sample size and key results were included in table 5. Of the 86 identified SRs and MAs, 24 studies reported cardiovascular diseases as outdoor air pollution related health outcomes, the figures of health service records and respiratory diseases studies that had been reported as an adverse effect of outdoor air pollution exposure were 22 and 19 respectively. Each of the rest five

groups of health outcomes accounted for an average SRs and MAs of 4. All SRs and MAs included more than 10 primary studies at least, health outcomes in all ages accounted for the largest groups in all categories, except for those of respiratory diseases category, in which children were the most suffered ones.

Overall, combinations of multiple pollutants were the dominant type of outdoor air pollution, which tended to show a harmful effect in all groups. What's more, it was the main cause of respiratory diseases among children and chronic diseases among people in all ages.

EGMs visualization

The feature of EGMs is to provide a visual display of evidence from the SRs and MAs. A bubble plot was used to display the types of air pollution and related health outcomes in a two-dimensional matrix framework, as presents in figure 4. The colours of bubbles in the map represented the confidence of SRs and MAs, which were assessed by the SURE checklist.[25] The red colour of bubbles represented low confidence and the yellow colour of bubbles meant medium confidence. The size of bubbles indicated the relative number of included studies, a larger bubble represented a larger study sample size in each grid. The confidence result of identified studies is shown in supplemental table s3. There was no green bubble in our EGM, which meant the high-quality SRs and MAs were in urgent need. What's more, there was a correlation between the study sample size and research quality.

Table 5 Characteristics of included SRs and MAs based on health outcome groups

Health outcome group (number of SRs and MAs)	Types of air pollution [a] (number of SRs and MAs)	Number of primary studies (mean +/- STD)	Population group (number of SRs and MAs)	Sample size (range)	Key results
Cardiovascular diseases (24)	Fine particulate matter (10) General air pollution gas (1) combinations of multiple pollutants (13)	32 +/- 30	Infant & children (1) Adults & old (5) All ages (16) Other (2)	（83, 11,850,884）	Positive (22) Ambiguous (2)
Chronic diseases (2)	combinations of multiple pollutants (2)	11 +/- 2	All ages (2)	（402, 62,012）	Positive (2)
Health service records (22)	Fine particulate matter (10) General air pollution gas (4) Other toxic substances (1) Mixed air pollution (7)	40 +/- 38	Infant & children (1) Adults & old (1) All ages (15) Other (5)	（1,050, 50,756,699）	Positive (21) Negative (1)
Cancer (4)	Fine particulate matter (1) combinations of multiple pollutants (3)	24 +/- 10	Adult (1) All ages (3)	（29, 500,000）	Positive (4)
Mental Disorders (5)	General air pollution gas (1) Other toxic substances (1) Mixed air pollution (3)	16 +/- 10	Infant & children (2) All ages (2) Other (1)	（252, 7,203）	Positive (3) Negative (1) Ambiguous (1)
Respiratory diseases (19)	Fine particulate matter (3) Other toxic substances (1) combinations of multiple pollutants (15)	37 +/- 31	Infant & children (11) Adults & old (1) All ages (6) Other (1)	（186, 1,146,215）	Positive (18) Negative (1)
Pregnancy & children (6)	Fine particulate matter (2) combinations of multiple pollutants (4)	23 +/- 22	Infant & children (1) All ages (3) Other (2)	（263, 3,545,177）	Positive (6)
Other diseases (4)	Fine particulate matter (2) Other toxic substances (1) combinations of multiple pollutants (1)	35 +/- 48	Adults & old (1) All ages (2) Other (1)	（73, 2,381,292）	Positive (3) Negative (1)

SRs and MAs, systematic reviews and meta-analyses.

combinations of multiple pollutants are the mixture of two or more air pollutants as followings: O3, SO2, CO, NO2, PM2.5, PM10, suspended particulate matter and total suspended particle.

DISCUSSION

This EGM provides the most up-to-date SRs and MAs by using the user-friendly visualization of the existing evidence in a matrix format of interventions and outcomes framework, so that it helps to set potential research agendas and to promote evidence-based policy makings. EGM is a novel evidence synthesized method in that it offers a reliable means of covering a broad scope of a particular sector, focusing on visualizing the quality of the existing evidence in a user-friendly format. Most importantly, EGM can address evidence gaps for funding research with limited resources and provide evidence-based information to support precise policy-making.

Most studies reported the health outcomes of cardiovascular diseases, respiratory diseases and health service records, which were mainly affected by fine particulate matter or combinations of multiple pollutants. While little studies investigated other toxic substances and its adverse effect on human-related health outcomes. By identifying the evidence gaps that existed in the outdoor air pollution related health outcomes, more potential research agendas need to focus on chronic diseases, cancer and mental disorders, so that research gaps can be filled and evidence-based information can be provided by meta analysis. By highlighting the confidence of the existing evidence based on inclusive studies, policymakers can promote relevant policies based on the existing summarised evidence of outdoor air pollution related health outcomes. In addition, more high-quality SRs and MAs, primary studies and synthesized evidence across a range of disciplines are needed to ensure the confidence of existing evidence for policy decision making.

This EGM is to comprehensively collect and categorize a variety body of SRs and MAs to overview the health outcomes affected by outdoor air pollution. However, the quality of 86 included SRs and MAs are either medium or low. The visualized categories of outdoor air pollution and health outcomes reveal the research gaps and concentrations of the existing literature. The health outcomes that are mostly studied in outdoor air pollution research often concentrate on cardiovascular diseases, respiratory diseases and health service records, including chronic obstructive pulmonary disease (COPD), blood pressure (BP), hypertension, asthma, morbidity and mortality. Most researchers and even the publics are concerned about these diseases. The major air pollution types are fine particulate matter ($PM_{2.5}$ and PM_{10}) and general air pollution gas (CO, SO_2, NO_2 and O_3), few health outcome studies are caused by other toxic air pollutants. These measurements of air pollutants, as air quality standards developed by the U.S. government in the 1970s, sometimes measured by different methods in other countries. This will induce some biases. Well-designed primary studies and meta analyses on chronic diseases, cancer, especially mental disorders are needed. People with chronic diseases, such as diabetes or COPD, are more susceptible to air pollution. These chronic diseases are also age-related. The health outcomes of these patients affected by air pollution are worthy of further investigation.

Some research gaps have been explored in this EGM. A major gap observed is the lack of definite diagnostic criteria of diseases. Criteria and reporting of air pollution related health

outcomes are notably variable, with significant potential for subject heterogeneity. Future research should define and report the diagnostic criteria more precisely. What's more, there are difficulties in estimating the personal exposure of air pollution. The heterogeneity of air pollution exposure levels, which are both in the primary studies and meta analyses, may probably lead to the "exposure bias". Although more and more primary studies began to use the measurement of exposure time, there is still room to use more precise estimation, such as wearable sensor applications. Another research gap we found is that the studies' period of SRs was not clearly reported. The air pollution levels are different in different time periods. Even in the same country or region, the levels of industrialization and modernization are different, which makes air pollution effects different. These SRs and MAs should be updated, and the time period of SRs and MAs should also be clearly reported. The "population bias" gap was also found in our EGMs. When including more children, for example, it could have overestimated the true prevalence of the diseases. Clearly stratified analysis of different age groups is needed for the reason that outdoor air pollution has different impact on different age groups.

Some important areas of air pollution research are left blank in the EGM. For example, few of the SRs included healthcare costs related to outdoor air pollution. As the public focus on environmental sustainability become even stronger in recent years, the demand for studies may increase. Moreover, they should come as a warning to policymakers as they show actual evidence for the healthcare costs related to outdoor air pollution. More precisely, studies aim at the economic burden of outdoor air pollution are needed.

Most included SRs and MAs estimated the health outcomes affected by outdoor air pollution in general population rather than those with established disease, thus, summarisation of the existing body of evidence should therefore be viewed in more research that aims at evaluating the health outcomes of established diseases affected by outdoor air pollution. Besides, research focuses on the physiological effects, such as increased heart rates and feelings of anxiety, which are indispensable so that EGM can capture a comprehensive overview of air pollution related health outcomes. Geographically, it is worth noting that most of the available primary studies included in SRs and MAs were conducted in western countries, where the median $PM_{2.5}$ concentration is less than 20 $\mu g/m^3$. In developing countries (such as China and India), however, the $PM_{2.5}$ concentrations in urban cities are likely to be up to 100$\mu g/m^3$, which have made a great impact on the local environment and people's health outcomes. The location of the primary study is an impact factor related to air pollution, and it should be considered with caution in both epidemiological studies and systematic reviews. There is room for more robust impact evaluation in the process of systematic reviews by using subgroup analysis.

There have some research gaps in current research of air pollution effects on people's health outcomes. Uniform diagnostic criteria of diseases, timely updating well-designed primary studies in local countries, and rational sampling (elders, children and patients with chronic diseases)

should be considered with caution during the evidence-based policy decision making process. These factors will affect the research outcomes by inducing some unobserved bias.

Limitations

Our EGM built on the evidence from significant numbers of SRs and MAs that have quantitatively addressed the health outcomes influenced by air pollution. The "gold standard" restriction on included studies may neglect important information available from studies. Since the main purpose of our EGMs is to provide a resource for policymakers, only the inclusion of SRs and MAs is sufficient to generate reliable conclusions.[20] Hundreds of quality appraisal methods exist in the research synthesis studies,[26] the efficiency of these studies depend largely on the quality assessment results, we only applied SURE checklist instead of other quality assessment methods in that it is more suitable for EGMs. Two reviewers assessed separately to prevent any bias occurred.

Only English-language SRs and MAs were included in our EGM, thus possibly missing pertinent information written in other languages. Primary studies, such as observational studies, time-series studies and causal inference studies, were not included for the reason that systematic level evidence has been comprehensively collected from the current research. In addition, this EGM largely relied on information provided by included SRs and MAs, there may have been some undetected errors of data extraction or research synthesis. Finally, research gaps identified in this EGM do not necessarily equate to research needs. It should consider the desirability, feasibility and importance of the research gaps, highlighting the importance of stakeholder engagement in this process.

CONCLUSIONS

This EGM provides a visual overview of health outcomes affected by outdoor air pollution. Despite the outlined limitations, it is a useful tool to inform environmental policy decision-makers. It also can promote further potential research by visualizing and synthesizing high-quality SRs and highlighting the absolute gaps. More prospective studies, with large numbers of participants, are needed in developing countries. It will be helpful to assess the long-term effects of air pollution more precisely.

Contributorship statement Zhuanlan Sun formulated the research question. Demi Zhu and Zhuanlan Sun devised the search strategy, consulting with experts from the Committee on Public Health and Urban Environment Management in China. Demi Zhu and Zhuanlan Sun conducted the search, screened all titles, abstracts and full articles and extracted data. Demi Zhu and Zhuanlan Sun co-wrote the manuscript.

Competing interests None declared.

Funding This work was supported by a major project of the National Social Science Fund of China grant number 13&ZD176.

Data sharing statement All data relevant to the EGM are included in the manuscript.

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FIGURE LEGEND

Figure 1 Systematic literature search process for eligible SRs and MAs. SRs, systematic reviews; MAs, meta analyses.

Figure 2 Regions and countries' distribution of eligible SRs and MAs.

The data of regions and countries are based on the information of corresponding authors. SRs, systematic reviews; MAs, meta analyses.

Figure 3 Numbers of inclusive eligible SRs and MAs in six research fields between 2004 and 2018.

The number of eligible SRs and MAs saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years. SRs, systematic reviews; MAs, meta analyses.

Figure 4 EGM for health outcomes affected by outdoor air pollution. The colours of bubbles represent the confidence of included SRs and MAs, red colour represents low confidence and yellow colour represents medium confidence. The size of the bubbles indicates the relative number of included SRs and MAs, and a larger bubble represents a larger study sample size in each grid. SRs, systematic reviews; MAs, meta analyses.

TABLE LEGEND

Table 1 Inclusion and exclusion criteria used in this EGM for eligible SRs and MAs.

Table 2 Information to be collected during the data extraction stage.

Table 3 General descriptions for included SRs and MAs.

Table 4 The categorized list of health outcomes.

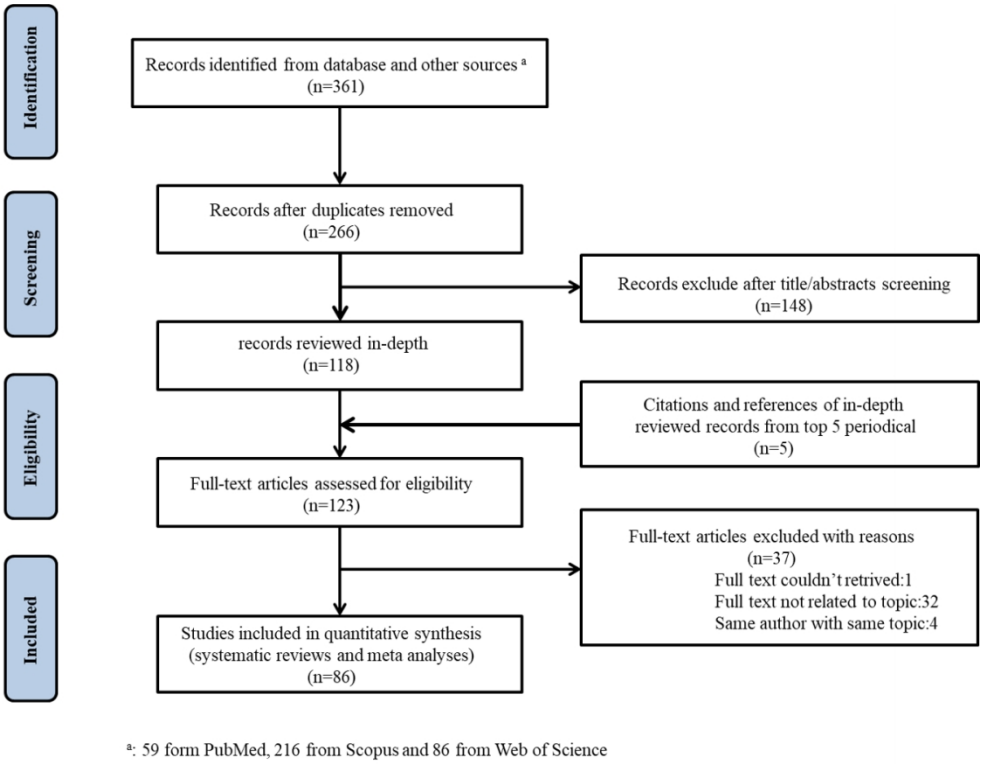
Table 5 Characteristics of included studies based on health outcome groups.

Supplemental Table S1 List of outdoor air pollution and health outcome related terms.

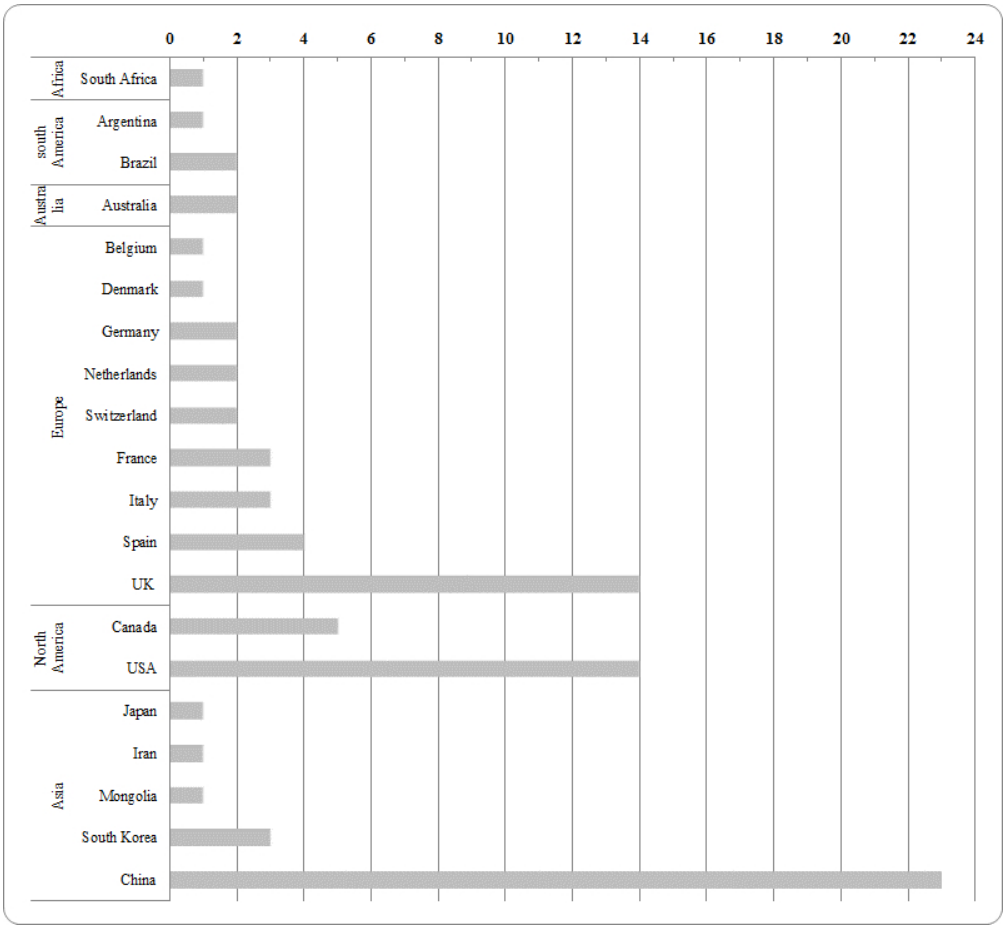
Supplemental Table S2 Search strategies for potentially relevant studies.

Supplemental Table S3 Confidence result of identified eligible SRs and MAs.

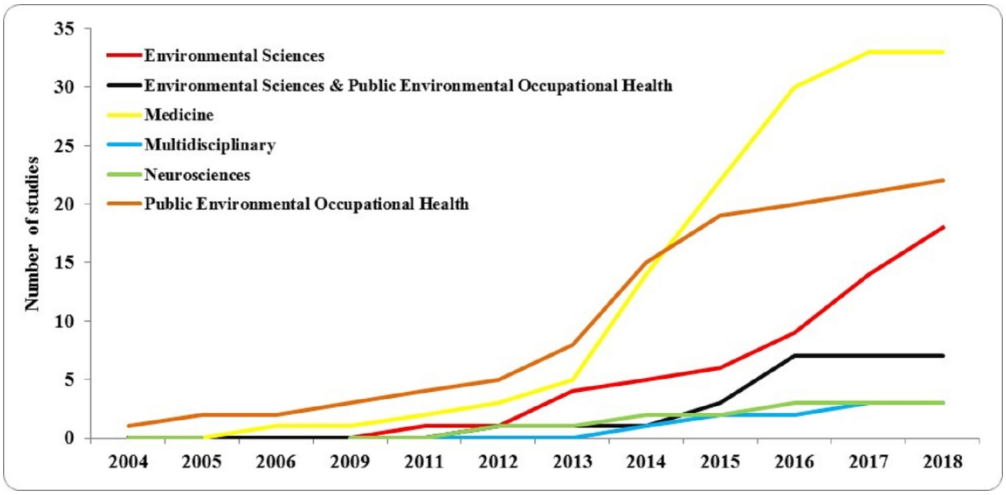
The list includes outdoor air pollution categories, health outcomes categories and the confidence result based on SURE.



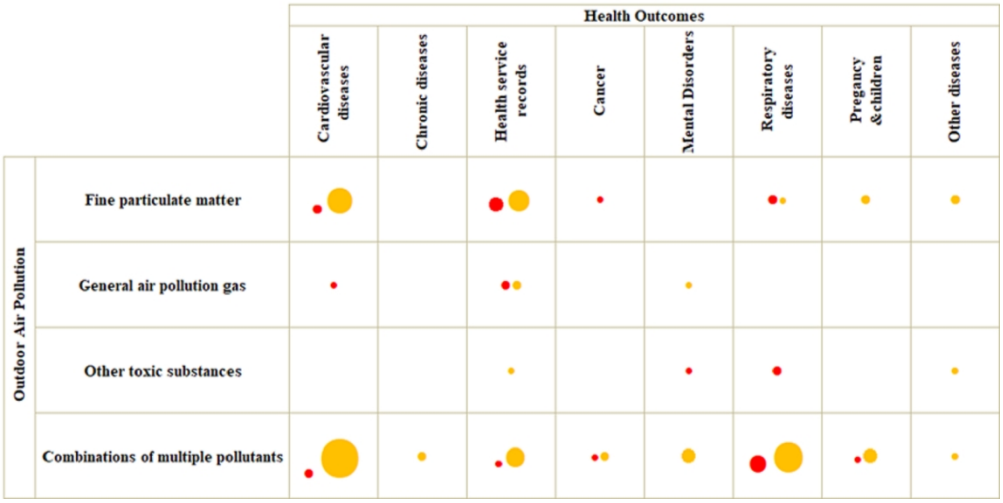
Systematic literature search process for eligible SRs and MAs. SRs, systematic reviews; MAs, meta analyses.



Regions and countries distribution of eligible SRs and MAs. The data of regions and countries are based on the information of corresponding authors. SRs, systematic reviews; MAs, meta analyses.



Numbers of inclusive eligible SRs and MAs in six research fields between 2004 and 2018. The number of the eligible SRs and MAs saw an increasing trend from 2004 to 2018. Most of the included studies were published in the recent six years. SRs, systematic reviews; MAs, meta analyses.



EGM for health outcomes affected by outdoor air pollution. The colours of bubbles represent the confidence of included SRs and MAs, red colour represents low confidence and yellow colour represents medium confidence. The size of the bubbles indicates the relative number of included SRs and MAs, and a larger bubble represents a larger study sample size in each grid. SRs, systematic reviews; MAs, meta analyses.

Supplemental Table S1:

List of outdoor air pollution and health outcome related terms.

Concept	Type	Detail
Outdoor air pollution	General air pollution gas	Ozone(O_3), sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen dioxide (NO_2)
	Fine particulate matter	Total suspended particle, suspended particulate matter, $PM_{2.5}$, PM_{10}
	Other toxic substances	Toxic air pollutants, volatile organic pollutants, nitrogen oxides (NO_x)
Health outcomes	Respiratory diseases	Asthma, lung cancer, respiratory infections, respiratory disorder
	Chronic diseases	Diabetes, chronic obstructive pulmonary disease
	Cardiovascular diseases	Hypertension, heart rate variability, heart attack, cardiopulmonary disease, ischemic heart disease, blood coagulation, deep vein thrombosis, stroke
	Health records	Morbidity, hospital admissions, outpatient visits, ER visits and mortality
	Other diseases	DNA methylation changes, neurobehavioral functions, inflammatory disease, skin disease, abortion, Alzheimer's disease, disability, cognitive function, Parkinson's disease

O_3, Ozone; SO_2, sulfur dioxide; CO, carbon monoxide; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; ER, emergence room.

Supplemental Table S2 [a]:

Search strategies for the potentially relevant studies.

1. Database and time period

PubMed Clinical Queries Database – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	Search ((((((((((Ozone*[MeSH Terms]) OR sulfur dioxide*[MeSH Terms]) OR carbon monoxide*[MeSH Terms]) OR nitrogen dioxide*[MeSH Terms]) OR PM2.5[MeSH Terms]) OR PM10[MeSH Terms]) OR total suspended particle*[MeSH Terms]) OR suspended particulate matter*[MeSH Terms]) OR Toxic air pollutant*[MeSH Terms]) OR volatile organic pollutant*[MeSH Terms]) OR nitrogen oxide*[MeSH Terms]	138,175
#2	Search ((((((((((((((((((((((((((asthma[MeSH Terms]) OR lung cancer[MeSH Terms]) OR respiratory infection*[MeSH Terms]) OR respiratory disorder*[MeSH Terms]) OR diabetes[MeSH Terms]) OR chronic respiratory disease*[MeSH Terms]) OR chronic obstructive pulmonary disease*[MeSH Terms]) OR hypertension[MeSH Terms]) OR heart rate variability[MeSH Terms]) OR heart attack[MeSH Terms]) OR cardiopulmonary disease*[MeSH Terms]) OR ischemic heart disease*[MeSH Terms]) OR blood coagulation*[MeSH Terms]) OR deep vein thrombosis[MeSH Terms]) OR stroke[MeSH Terms]) OR morbidity[MeSH Terms]) OR hospital admission*[MeSH Terms]) OR outpatient visit*[MeSH Terms]) OR emergency room visit*[MeSH Terms]) OR mortality[MeSH Terms]) OR DNA methylation change*[MeSH Terms]) OR neurobehavioral function[MeSH Terms]) OR Inflammatory disease*[MeSH Terms]) OR skin disease*[MeSH Terms]) OR abortion[MeSH Terms]) OR Alzheimer's disease*[MeSH Terms]) OR	3,125,123

item	Search input	result
	disability[MeSH Terms]) OR cognitive function[MeSH Terms]) OR Parkinson's disease*[MeSH Terms]	
#3	Search (outdoor[Text Word]) AND air pollution[Text Word]	3,132
#4	meta analysis[Title/Abstract]	111,455
	#1 AND #2 AND #3 AND #4	0
	#3 AND #4	**44**
#5	systematic review[Title/Abstract]	111,428
	#1 AND #2 AND #3 AND #5	0
	#3 AND #5	**38**

After duplication: 59

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1. Database and time period

Scopus – inception-6/24/2018

2. Language:

English

3. Search strategy:

item	Search input	result
#1	TITLE-ABS-KEY ("Ozone*") OR TITLE-ABS-KEY ("sulfur dioxide*") OR TITLE-ABS-KEY ("carbon monoxide*") OR TITLE-ABS-KEY ("nitrogen dioxide*") OR TITLE-ABS-KEY (pm2.5) OR TITLE-ABS-KEY (pm10) OR TITLE-ABS-KEY (total AND suspended AND particle*) OR TITLE-ABS-KEY (suspended AND particulate AND matter*) OR TITLE-ABS-KEY (toxic AND air AND pollutant*) OR TITLE-ABS-KEY ("volatile organic pollutant*") OR TITLE-ABS-KEY ("nitrogen oxide*")	327,759
#2	TITLE-ABS-KEY ("asthma") OR TITLE-ABS-KEY ("lung cancer") OR TITLE-ABS-KEY ("respiratory infection*") OR TITLE-ABS-KEY ("respiratory disorder*") OR TITLE-ABS-KEY ("diabetes*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("chronic obstructive pulmonary disease*") OR TITLE-ABS-KEY ("hypertension") OR TITLE-ABS-KEY ("heart rate variability") OR TITLE-	4,445,123

item	Search input	result
	ABS-KEY ("heart attack") OR TITLE-ABS-KEY ("cardiopulmonary disease*") OR TITLE-ABS-KEY ("ischemic heart disease*") OR TITLE-ABS-KEY ("blood coagulation") OR TITLE-ABS-KEY ("deep vein thrombosis") OR TITLE-ABS-KEY (stroke) OR TITLE-ABS-KEY (morbidity) OR TITLE-ABS-KEY (" hospital admission*") OR TITLE-ABS-KEY ("outpatient visit*") OR TITLE-ABS-KEY (" emergency room visit*") OR TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (" DNA Methylation Change*") OR TITLE-ABS-KEY ("neurobehavioral function*") OR TITLE-ABS-KEY (" Inflammatory disease* ") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (abortion) OR TITLE-ABS-KEY ("Alzheimer's disease*") OR TITLE-ABS-KEY ("skin disease*") OR TITLE-ABS-KEY (disability) OR TITLE-ABS-KEY ("cognitive function") OR TITLE-ABS-KEY ("Parkinson's disease*")	
#3	ALL (outdoor) AND ALL (" air pollution*")	31,240
#4	TITLE-ABS-KEY ("meta analysis*") OR TITLE-ABS-KEY ("systematic review*")	330,816
	#1 AND #2 AND #3 AND #4	**216**

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1. Database and time period

Web of science– inception-6/24/2018

2. Language:

English

3. Search strategy:

item	search	result
#1	TS = (Ozone* OR sulfur dioxide* OR carbon monoxide* OR nitrogen dioxide* OR PM2.5 OR PM10 OR total suspended particle* OR suspended particulate matter* OR Toxic air pollutant* OR volatile organic pollutant OR nitrogen oxide*)	674,294

item	search	result
#2	TS = (asthma OR lung cancer OR respiratory infection* OR respiratory disorder* OR diabetes OR chronic respiratory disease* OR chronic obstructive pulmonary disease* OR hypertension OR heart rate variability OR heart attack OR cardiopulmonary disease* OR ischemic heart disease* OR blood coagulation* OR deep vein thrombosis OR stroke OR morbidity OR hospital admission* OR outpatient visit* OR emergency room visit* OR mortality OR DNA methylation change* OR neurobehavioral function OR Inflammatory disease* OR skin disease* OR abortion OR Alzheimer's disease* OR disability OR cognitive function OR Parkinson's disease*)	7,157,410
#3	TS = (outdoor AND air pollution*)	10,814
#4	TS = ("meta analysis ")	174,699
	#1 AND #2 AND #3 AND #4	**53**
#5	TS = ("systematic review ")	163,736
	#1 AND #2 AND #3 AND #5	**33**

[a]: Database Cochrane search result was zero.

Supplemental Table S3:
Confidence result of identified eligible SRs and MAs.

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yang et al (2018)[1]	Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Zhao et al (2018)[2]	Ambient ozone exposure and mental health: A systematic review of epidemiological studies	Germany	General air pollution gas	Mental disorders	Medium
Newell et al (2018)[3]	Cardiorespiratory health effects of gaseous ambient air pollution exposure in low and middle income countries: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Health Records	Medium
An et al (2018)[4]	Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis	America	Mixed air pollution	Other diseases	Medium
Zhang, Wang & Lu (2018)[5]	Exposure to nitrogen dioxide and chronic obstructive pulmonary disease (COPD) in adults: a systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
DeVries, Kriebel & Sama (2017)[6]	Outdoor Air Pollution and COPD-Related Emergency Department Visits, Hospital Admissions, and Mortality: A Meta-Analysis	America	Mixed air pollution	Health Records	Medium
Khreis et al (2017)[7]	Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Fajersztajn et al (2017)[8]	Short-term effects of fine particulate matter pollution on daily health events in Latin America: a systematic review and meta-analysis	Brazil	Fine particulate matter	Health Records	Medium
Huang et al (2017)[9]	Relationship between exposure to PM2.5 and lung cancer incidence and mortality: A meta-analysis	China	Fine particulate matter	Health Records	Medium
Nguyen Thi Trang et al (2017)[10]	Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-series and case-crossover studies	Switzerland	Mixed air pollution	Respiratory diseases	Medium
Orellano et al (2017)[11]	Effect of outdoor air pollution on asthma exacerbations in children and adults: Systematic review and multilevel meta-analysis	Argentina	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Zhao et al (2017)[12]	The impact of short-term exposure to air pollutants on the onset of out-of-hospital cardiac arrest: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Achilleos et al (2017)[13]	Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis	America	Fine particulate matter	Health Records	Low
Ngoc et al (2017)[14]	Systematic review and meta-analysis of human skin diseases due to particulate matter	South Korea	Fine particulate matter	Other diseases	Medium
Lin et al (2017)[15]	Lung cancer mortality of residents living near petrochemical industrial complexes: a meta-analysis	China	Other toxic substances	Health Records	Medium
Froes Asmus et al (2016)[16]	A Systematic Review of Children's Environmental Health in Brazil	Brazil	Mixed air pollution	Respiratory diseases	Low
Zhang et al (2016b)[17]	Association between atmospheric particulate matter and adverse pregnancy outcomes in the population	China	Fine particulate matter	Pregnancy & children	Medium
Lim et al (2016)[18]	Short-term effect of fine particulate matter on children's hospital admissions and emergency department visits for asthma: A systematic review and meta-analysis	South Korea	Fine particulate matter	Respiratory diseases	Medium
Mills et al (2016)[19]	Distinguishing the associations between daily mortality and hospital admissions and nitrogen dioxide from those of particulate matter: A systematic review and meta-analysis	United Kingdom	General air pollution gas	Health Records	Medium
Fan et al (2016)[20]	The impact of PM2.5 on asthma emergency department visits: a systematic review and meta-analysis	China	Fine particulate matter	Health Records	Medium
Bloemsma, Hoek & Smit, 2016)[21]	Panel studies of air pollution in patients with COPD: Systematic review and meta-analysis	Netherlands	Fine particulate matter	Cardiovascular diseases	Medium
Li et al (2016)[22]	Major air pollutants and risk of COPD exacerbations: A systematic review and meta-analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Franchini et al (2016)[23]	Association between particulate air pollution and venous thromboembolism: A systematic literature review	Italy	Fine particulate matter	Cardiovascular diseases	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Pascal et al (2016)[24]	The mortality impacts of fine particles in France	France	Fine particulate matter	Health Records	Medium
Checa Vizcaino et al (2016)[25]	Outdoor air pollution and human infertility: a systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Power et al (2016)[26]	Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research	America	Mixed air pollution	Mental disorders	Medium
Song et al (2016)[27]	Short-term exposure to air pollution and cardiac arrhythmia: A meta-analysis and systematic review	China	Mixed air pollution	Cardiovascular diseases	Medium
Flores-Pajot et al (2016)[28]	Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: A review and meta-analysis	Canada	Mixed air pollution	Mental disorders	Medium
Hou et al (2016)[29]	The role of the PM2.5-associated metals in pathogenesis of child Mycoplasma Pneumoniae infections: a systematic review	China	Fine particulate matter	Respiratory diseases	Low
Zhang et al (2016a)[30]	Short-term exposure to air pollution and morbidity of COPD and asthma in East Asian area: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2016)[31]	Impact of air quality guidelines on COPD sufferers	America	Mixed air pollution	Cardiovascular diseases	Medium
Cai et al (2016)[32]	Associations of Short-Term and Long-Term Exposure to Ambient Air Pollutants With Hypertension: A Systematic Review and Meta-Analysis	China	Mixed air pollution	Cardiovascular diseases	Medium
Luo et al (2015)[33]	Short-term exposure to particulate air pollution and risk of myocardial infarction: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2015)[34]	Fine particle components and health - A systematic review and meta-analysis of epidemiological time series studies of daily mortality and hospital admissions	United Kingdom	Mixed air pollution	Health Records	Low
Hamra et al (2015)[35]	Lung cancer and exposure to nitrogen dioxide and traffic: A systematic review and meta-analysis	America	Mixed air pollution	Cancer	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Chen et al (2015)[36]	Traffic-related air pollution and lung cancer: A meta-analysis	China	Mixed air pollution	Cancer	Medium
Jadambaa et al (2015)[37]	The impact of the environment on health in Mongolia: A systematic review	Mongolia	Mixed air pollution	Respiratory diseases	Low
Eze et al (2015)[38]	Association between ambient air pollution and diabetes mellitus in Europe and North America: Systematic review and meta-analysis	Switzerland	Mixed air pollution	Chronic diseases	Medium
Nurmatov et al (2015)[39]	Volatile organic compounds and risk of asthma and allergy: A systematic review	United Kingdom	Other toxic substances	Respiratory diseases	Low
Cui et al (2015)[40]	Ambient particulate matter and lung cancer incidence and mortality: A meta-analysis of prospective studies	China	Fine particulate matter	Health Records	Medium
Rodriguez-Villamizar et al (2015)[41]	The effects of outdoor air pollution on the respiratory health of Canadian children: A systematic review of epidemiological studies	Canada	Mixed air pollution	Respiratory diseases	Low
Bowatte et al (2015)[42]	The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: A systematic review and a meta-analysis of birth cohort studies	Australia	Mixed air pollution	Respiratory diseases	Medium
Shah et al (2015)[43]	Short term exposure to air pollution and stroke: Systematic review and meta-analysis	United Kingdom	Mixed air pollution	Cardiovascular diseases	Medium
Scheers et al (2015)[44]	Long-Term Exposure to Particulate Matter Air Pollution Is a Risk Factor for Stroke: Meta-Analytical Evidence	Belgium	Fine particulate matter	Cardiovascular diseases	Medium
Filippini et al (2015)[45]	A review and meta-analysis of outdoor air pollution and risk of childhood leukemia	Italy	Mixed air pollution	Cardiovascular diseases	Low
Frutos et al (2015)[46]	Impact of air pollution on fertility: A systematic review	Spain	Mixed air pollution	Pregnancy & children	Medium
Zheng et al (2015)[47]	Association between Air pollutants and asthma emergency room visits and hospital admissions in time series studies: A systematic review and meta-Analysis	China	Mixed air pollution	Health Records	Medium
Liu et al (2015)[48]	Association of exposure to particular matter and carotid intima-media thickness: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Balti et al (2014)[49]	Air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis	South Africa	Mixed air pollution	Chronic diseases	Medium
Faustini, Rapp & Forastiere (2014)[50]	Nitrogen dioxide and mortality: Review and meta-analysis of long-term studies	Italy	Mixed air pollution	Health Records	Medium
Li et al (2014)[51]	Mechanisms in endocrinology: Main air pollutants and diabetes-associated mortality: A systematic review and meta-analysis	China	Mixed air pollution	Health Records	Medium
Rossignol, Genuis & Frye (2014)[52]	Environmental toxicants and autism spectrum disorders: A systematic review	America	Other toxic substances	Mental disorders	Low
Hamra et al (2014)[53]	Outdoor particulate matter exposure and lung cancer: A systematic review and meta-analysis	France	Fine particulate matter	Cancer	Low
Hu et al (2014)[54]	Ambient air pollution and hypertensive disorders of pregnancy: A systematic review and meta-analysis	America	Mixed air pollution	Cardiovascular diseases	Medium
Pedersen et al (2014)[55]	Ambient air pollution and pregnancy-induced hypertensive disorders: A systematic review and meta-analysis	Spain	Mixed air pollution	Cardiovascular diseases	Medium
Bell, Zanobetti & Dominici (2014)[56]	Who is more affected by ozone pollution? A systematic review and meta-analysis	America	General air pollution gas	Health Records	Low
Shin et al (2014)[57]	Outdoor fine particles and nonfatal strokes: Systematic review and meta-analysis	America	Fine particulate matter	Cardiovascular diseases	Low
Song et al (2014)[58]	The global contribution of outdoor air pollution to the incidence, prevalence, mortality and hospital admission for chronic obstructive pulmonary disease: a systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Atkinson et al (2014)[59]	Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: A systematic review and meta-analysis	United Kingdom	Fine particulate matter	Health Records	Low
Dick et al (2014b)[60]	A systematic review of associations between environmental exposures and development of asthma in children aged up to 9 years	United Kingdom	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Yamamoto, Phalkey & Malik (2014)[61]	A systematic review of air pollution as a risk factor for cardiovascular disease in South Asia: Limited evidence from India and Pakistan	Germany	Mixed air pollution	Cardiovascular diseases	Medium
Chen et al (2014)[62]	Effects of air pollution on the risk of congenital anomalies: A systematic review and meta-analysis	France	Mixed air pollution	Mental disorders	Medium
Dick et al (2014a)[63]	Associations between environmental exposures and asthma control and exacerbations in young children: A systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Teng et al (2014)[64]	A systematic review of air pollution and incidence of out-of-hospital cardiac arrest	Australia	Mixed air pollution	Cardiovascular diseases	Low
Vawda et al (2014)[65]	Associations between inflammatory and immune response genes and adverse respiratory outcomes following exposure to outdoor air pollution: A huge systematic review	United Kingdom	Mixed air pollution	Respiratory diseases	Low
Yu et al (2014)[66]	Short-term effects of particulate matter on stroke attack: Meta-regression and meta-analyses	China	Fine particulate matter	Cardiovascular diseases	Medium
Liang et al (2014)[67]	Effect of exposure to PM2.5 on blood pressure: A systematic review and meta-analysis	China	Fine particulate matter	Cardiovascular diseases	Medium
Zhu et al (2013)[68]	The relationship between particulate matter (PM10) and hospitalizations and mortality of chronic obstructive pulmonary disease: A meta-analysis	China	Fine particulate matter	Health Records	Low
Hoek et al (2013)[69]	Long-term air pollution exposure and cardio-respiratory mortality: A review	Netherlands	Fine particulate matter	Health Records	Medium
Anderson, Favarato & Atkinson (2013a)[70]	Long-term exposure to outdoor air pollution and the prevalence of asthma: Meta-analysis of multi-community prevalence studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium
Anderson, Favarato & Atkinson (2013b)[71]	Long-term exposure to air pollution and the incidence of asthma: Meta-analysis of cohort studies	United Kingdom	Mixed air pollution	Respiratory diseases	Medium

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Bell, Zanobetti & Dominici (2013)[72]	Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis.	America	Fine particulate matter	Other diseases	Medium
Nieuwenhuijsen et al (2013)[73]	Environmental risk factors of pregnancy outcomes: a summary of recent meta-analyses of epidemiological studies.	Spain	Fine particulate matter	Pregnancy & children	Medium
Mehta et al (2013)[74]	Ambient particulate air pollution and acute lower respiratory infections: A systematic review and implications for estimating the global burden of disease	America	Mixed air pollution	Respiratory diseases	Medium
Park, Bae & Hong (2013)[75]	PM10 exposure and non-accidental mortality in Asian populations: A meta-analysis of time-series and case-crossover studies	South Korea	Fine particulate matter	Health Records	Medium
Stieb et al (2012)[76]	Ambient air pollution, birth weight and preterm birth: A systematic review and meta-analysis	Canada	Mixed air pollution	Pregnancy & children	Medium
Gasana et al (2012)[77]	Motor vehicle air pollution and asthma in children: A meta-analysis	America	Mixed air pollution	Respiratory diseases	Medium
Li et al (2012)[78]	Meta-Analysis of Association between Particulate Matter and Stroke Attack	China	Fine particulate matter	Cardiovascular diseases	Medium
Takenoue et al (2012)[79]	Influence of outdoor NO2 exposure on asthma in childhood: Meta-analysis	Japan	General air pollution gas	Health Records	Medium
Tashakkor, Chow & Carlsten, 2011)[80]	Modification by antioxidant supplementation of changes in human lung function associated with air pollutant exposure: A systematic review	Canada	Other toxic substances	Respiratory diseases	Low
Afshari et al (2011)[81]	Inhaled nitric oxide for acute respiratory distress syndrome and acute lung injury in adults and children: A systematic review with meta-analysis and trial sequential analysis	Denmark	Other toxic substances	Other diseases	Medium
Shah, Balkhair & Knowledge Synth Grp Determinants (2011)[82]	Air pollution and birth outcomes: A systematic review	Canada	Mixed air pollution	Pregnancy & children	Low

Author(s) and Year	Title of Publication	Country	Outdoor air pollution	Health Outcomes	Confidence result based on SURE
Forbes et al (2009)[83]	Chronic exposure to outdoor air pollution and diagnosed cardiovascular disease: meta-analysis of three large cross-sectional surveys.	United Kingdom	General air pollution gas	Cardiovascular diseases	Low
Mahjub & Gh (2006)[84]	Meta-analysis of case-referent studies of specific environmental or occupational pollutants on lung cancer	Iran	Mixed air pollution	Cancer	Medium
Ito, De Leon & Lippmann (2005)[85]	Associations between ozone and daily mortality: Analysis and meta-analysis	America	General air pollution gas	Health Records	Low
Ward & Ayres (2004)[86]	Particulate air pollution and panel studies in children: a systematic review.	United Kingdom	Fine particulate matter	Respiratory diseases	Low

SRs, systematic reviews; MAs, meta analyses.

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