BMJ Open

Ambient air pollution and birth outcomes: a scoping review to investigate the mediating and moderating variables—protocol

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To cite: Perry L, Mizen A, Ellis-Davies K, *et al*. Ambient air pollution and birth outcomes: a scoping review to investigate the mediating and moderating variables—protocol. *BMJ Open* 2025;**15**:e088477. doi:10.1136/bmjopen-2024-088477

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-088477).

Received 07 May 2024
Accepted 17 January 2025

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ABSTRACT

Introduction Pregnant women and their babies are a highly vulnerable population to health effects from air pollution. This scoping review aims to understand the extent and type of evidence concerning the mediating and moderating factors between air pollution and birth outcomes. By gathering and synthesising this evidence, this review aims to identify key concepts, themes and knowledge gaps. In turn, these findings will serve as a valuable resource for researchers and policymakers by highlighting potential pathways and gaps in evidence.

Methods and analysis This scoping review protocol is based on the Joanna Briggs Institute (JBI) methodology for scoping reviews and will be reported in full with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping review (PRISMA-ScR) flow diagram. This review will search eight databases: Web of Science, Scopus, PubMed, Embase, GreenFILE, CINAHL Ultimate, APA PsycINFO and MIDIRS. Results will be limited to those written or translated into English and peer-reviewed studies with no restriction on publication date. The study selection and data extraction will be completed within the software Covidence by two or more independent reviewers, with conflicts solved by group discussion. The data extracted from this process will include publication details, study characteristics and population characteristics.

Ethics and dissemination This study will not collect primary data; therefore, no formal ethical approval is required. The findings will be disseminated to academic and non-academic audiences through conferences, publications and focus groups.

Trail registration number Open Science Framework (https://doi.org/10.17605/OSF.IO/6Y2D9).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This review will search eight databases from multiple disciplines to gain a thorough understanding of the available evidence.
⇒ This review is guided by PRISMA-ScR guidelines and conducted according to JBI methodology for scoping reviews—a validated methodological framework.
⇒ The review will be limited to peer-reviewed articles in the English language.

INTRODUCTION

Background

Air pollution is a major global problem, with growing evidence indicating strong associations with health issues such as asthma, cardiovascular diseases, lung cancer and more.[1] With greater research into the relationship between ambient air pollution and health, the WHO updated its guidelines on individual exposure in 2021. Notably, the recommended maximum annual exposure of particulate matter 2.5 µg ($PM_{2.5}$) has halved since 2005.[2] Therefore, 99% of the global population is now considered to be living with exposure levels greater than the WHO guidelines.[3] While these guidelines aim to target policy on a large scale, interventions can also be implemented at an individual level or targeted to vulnerable groups. Research into the mechanisms behind the air pollution/health relationship will provide insight into potential points of intervention. Therefore, increasing personal autonomy and protecting the future population is essential.

Air pollution is often associated only with respiratory disease. The primary route for air pollution to enter the body is through inhalation, which can directly harm the respiratory tract.[4] Larger particulates, such as PM_{10}, are trapped in the upper airways.[5] However, smaller particles, like $PM_{2.5}$ and some gaseous pollutants, can travel further and reach the alveoli.[5 6] From here, the pollutants can diffuse from the lung tissues and into the bloodstream,[6] where they can be transported to almost every organ and tissue in the body.[7] While this review does not intend to provide a detailed enquiry on the biological mechanisms, it is essential to acknowledge air pollution's expansive threat to the body as it has the potential to cause harm to every physiological

system. This amplifies the hazardous nature of air pollution to population health.

Pregnant women and their fetuses are especially vulnerable to adverse health consequences resulting from air pollution. During pregnancy, oxygen consumption for the mother is 20% higher, suggesting that more air pollutants are inhaled due to increased tidal volume.[8] It has been theorised that fine particulate matter can be passed from mother to fetus across the placental barrier thus having the potential to affect all organs of the fetus.[9] These factors mean that pregnant women and their fetuses are disproportionately affected by air pollution and should be a major focus in future policy regarding air pollution.

Physiological changes in pregnancy are not limited to just the respiratory system. The cardiovascular and immune systems also experience extensive modifications. For the cardiovascular system, this includes a modified heart position, 40%–50% increased cardiac output and up to 20% increase in heart rate,[10] contributing to an overall increase of stress in the body. In addition, the immune system does not have a global suppression as previously thought;[11] instead, the position and amount of specific immune cells change.[12] This article noted as an example that the amount of neutrophils rises and monocytes become more active. Both these types of white blood cells are vital to defend against viruses and bacterial infections.[12] Therefore, changes in these delicately balanced systems further increase the vulnerability of the mother and fetus as more than one bodily system is under stress before considering exposure to air pollution.

Air pollution can affect pregnant women and their fetuses in various ways. Existing studies have investigated the links between air pollution exposure and preterm birth, low birth weight, stillbirth and infant mortality.[13] These adverse birth outcomes can have life-long impacts. Children who are subject to these outcomes have a greater risk of childhood disability and chronic illness.[14] This further indicates the need to better understand the causal pathways between air pollution and adverse birth outcomes. Devastating effects can potentially be decreased by reducing air pollution exposure or altering factors known to exacerbate its effects.

Rationale

The relationship between prenatal ambient air pollution exposure and adverse birth outcomes has been extensively investigated. In 2022, an umbrella review, which covered 36 systematic reviews and meta-analyses on the subject, was conducted.[15] The 295 primary studies captured within this umbrella review demonstrated a consistent pattern of association between air pollution during pregnancy and poor birth outcomes.[15] However, this umbrella review called for future research to address the causal mechanisms driving these relationships. Our scoping review aims to initiate efforts to address this gap in research by mapping the available evidence on this topic.

This scoping review will consider studies that include mediating and/or moderating effects between air pollution and birth outcomes. We aim to develop a scientific understanding of the pathways through which air pollution exerts its impacts on birth outcomes and highlight areas for further investigation. In turn, this may highlight interventions to mitigate the adverse effects of air pollution during and immediately after pregnancy.

A preliminary search of Web of Science, Scopus and the Cochrane Database of Systematic Reviews was conducted, and no existing or underway systematic or scoping reviews on this topic were identified. However, the search outputted a reasonable number of papers, leading us to believe that there was sufficient evidence for a scoping review. The initial search resulted in documents across multiple disciplines. Therefore, mediating and moderating factors are expected to span multiple categories, with prevalent themes being biological, environmental and social. Due to the broad and emerging nature of the research topic, a scoping review is best suited to map the available evidence and identify what mediating or moderating factors require further investigation.

Review question

The review draws on the population, concept and context framework to investigate 'What are the potential mediating and moderating variables that have been explored in the relationship between air pollution and birth outcomes?'. This framework is most appropriate as it provides flexibility to map the available knowledge on this topic and is in line with guidelines for scoping reviews.[16]

The overall research question will be answered within the following subquestions:

1. What birth outcomes have been reported in the mediation/moderation pathway?
2. What mediators and moderators have been investigated?
3. How and what types of air pollution are measured in these studies?
4. What are the sample characteristics and geographic location of these studies?
5. Which disciplines investigate these relationships?
6. What methods have been used to investigate these relationships?

METHODS AND ANALYSIS

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews.[16] We intend to conduct this study from January to June 2025.

Eligibility criteria

Population

This review will consider pregnant women and their babies only. The times of interest are during pregnancy (conception to delivery) and after delivery. This is not limited by geographical location or date range.

Concept

The concept refers to a separate variable that influences the relationship between air pollution and birth

outcomes. A mediating factor (or mediator) refers to the pathway in which two variables are related.[17] In a general form, a mediator is caused by the independent variable (IV), which sequentially impacts the dependent variable (DV).[18] The mediation variable may explain part or all of the relationship between the IV and DV. This can be tested within mediation analysis, enabling a greater understanding of the pathways between the IV and DV.

A moderating factor (or moderator) influences the strength and direction of a relationship between the variables of interest.[17] A moderator may also be referred to as an effect modifier.

This review does not aim to draw conclusions around the strength of effect these variables have. Instead, we aim to map out which mediating and moderating variables have been explored in past work. Therefore, we will include studies that hypothesise or statistically test these variables.

Context

The context refers to the relationship between ambient air pollution and adverse birth outcomes. The inclusion criteria for ambient air pollution will focus on major pollutants that have been examined in the past literature as a detriment to health, for example, particulate matter, nitrogen dioxide, nitrogen oxides, sulphur dioxides, ozone and carbon monoxide. Theoretically, while it is expected that indoor air pollution may have a greater influence on the population of interest, there are limited studies on indoor air pollution alone, and it is difficult to modify this exposure from a policy perspective. Therefore, outdoor air pollution is the exposure focus of this review.

This review will only consider post-birth outcomes such as preterm birth and low birth weight (complete list in table 1). While pre-birth outcomes such as spontaneous abortion are also important when considering the adverse effects of air pollution on pregnancy outcomes, our initial search returned minimal results on the subject. This is likely due to the data's sensitive nature, making it difficult to obtain. Hence, due to the limited studies on this area, it is not included in this review. This review will not exclude studies on the basis of which country they were conducted in.

Types of sources

This scoping review will consider any peer-reviewed primary study. Due to the dynamic nature of the research question and the expectation of research spanning multiple disciplines, including all types of primary study will provide a comprehensive overview. A full list of inclusion criteria for source selection is included within table 2.

Search strategy

The search strategy aims to locate published studies. An initial search limited to Web of Science and Scopus was undertaken to identify articles from multiple disciplines on this topic. Terms from the titles, abstracts and keywords were harvested to develop the final search strategy. This search strategy, including all identified keywords and indexed terms, will be adapted for each database. This is necessary due to the use of truncation within the search

Table 1 Population, concept and context framework

Framework	Inclusion	Exclusion
Population	Pregnant women and fetus Antenatal Postnatal Post-pregnancy Peripartum	Non-pregnant women
Concept	Mediator variables Mediation analysis Moderator variables Effect modifiers	Cofounders Covariates Studies without a mediating or moderating variable
Context	Ambient air pollution (outdoor) including the following: ► Particulate matter ($PM_{2.5}$ and PM_{10}) ► Nitrogen dioxide ► Nitrogen oxides ► Sulphur dioxide ► Ozone ► Carbon monoxide ► Non-methane volatile organic compounds ► Ammonia Post-birth outcomes, including the following: ► Preterm birth ► Low birth weight ► Small for gestational age ► Stillbirth ► Low APGAR Score ► Fetal growth restriction	Indoor air pollution Prebirth outcomes, such as spontaneous abortion

APGAR, Appearance, Pulse, Grimace, Activity and Respiration.

Table 2 Source selection criteria

Inclusion	Exclusion
Published or translated into English	Written in any language other than English
Peer-reviewed	Non-peer-reviewed work (grey literature) such as government reports, conference abstracts, theses and dissertations
Includes discussion or analyses on a mediating or moderating factor	Does not include a mediating or moderating factor
No geographical restrictions	
No date restrictions	

terms and the uniqueness of tools/features. Therefore, ensuring the search works correctly on each database.

Studies published or translated into English will be included. Studies from any date range will be included to capture a broad range of literature. Additionally, as there are no existing reviews on the specific research question to build on, it is necessary to capture everything.

The databases to be searched include Web of Science, Scopus, Embase, PubMed, MIDIRS, GreenFILE, CINAHL Ultimate and APA PsycINFO within EBSCOhost. These databases were selected after the initial search within Web of Science and Scopus which highlighted the range of disciplines that report on this topic and captured the mixed discipline studies. Embase, PubMed, MIDIRS and CINAHL Ultimate cover medical/health-based studies, while GreenFILE and APA PsycINFO are the primary databases to capture the environmental and psychological studies, respectively. A full search strategy for each database is included within the online supplemental materials.

Source selection

After completing the search, all identified citations will be collated and uploaded into Covidence,[19] and duplicates will be removed. Following a pilot test, titles and abstracts will then be screened by two or more independent reviewers for assessment against the inclusion criteria. Potentially relevant sources will be retrieved in full, and their citation details will be imported into Covidence. The full text of selected citations will be assessed in detail against the inclusion criteria by two or more independent reviewers. Reasons for excluding sources of evidence in full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through group discussion or a third reviewer. The results of the search and the study inclusion process will be reported in full in the final scoping review in a PRISMA-ScR flow diagram.[20]

Data extraction

Data will be extracted from papers included in the scoping review in Covidence by two or more independent reviewers. Any disagreements that arise between the reviewers will be resolved through discussion, or with an additional reviewer. If appropriate, authors of papers will be contacted to request missing or additional data, where required. The following information will be charted:

Publication details:

- Author(s).
- Year of publication.
- Geographical location.
- Journal name.
- Primary discipline.

Study characteristics:

- Study design.
- Study period.
- Data source/type.
- Methodology for measuring air pollution.
- Point of exposure during pregnancy (eg, whole pregnancy and first trimester).
- Type of birth outcomes measured and their definitions for each (eg, preterm birth, low birth weight and APGAR score).
- Details on mediation variables (tested or hypothesised).
- Details on moderation variables (tested or hypothesised).
- Methodology for effect moderation or mediation analysis where tested.
- Conclusions on mediating and moderating effect.
- Covariates in these studies, for example, pregnancy complications and maternal smoking status.

Population characteristics:

- Sample size.
- Maternal characteristics (eg, mean age, education, ethnicity and poverty level).

Data analysis and presentation

This review will report on the findings in the following ways; however, this may change once the review has been conducted as it cannot be foreseen what methods are most appropriate for the data:

- Global heat map indicating study location.
- Table of publication characteristics.
- Word cloud of mediators.
- Word cloud of moderators.
- Visual representation of birth outcomes.
- Visual representation of air pollutants investigated.

This will be followed by a narrative synthesis to expand and answer the subquestions. The above data presentation was guided by Pollock *et al*.[21]

ETHICS AND DISSEMINATION

This study is not subject to any formal ethical approval as no primary data is collected. Dissemination is planned for

both academic and non-academic audiences. We intend to publish the outcomes of this review in *BMJ Open* and present at various conferences during the process of this review and once completed to gain feedback on our methodology throughout.

This review will inform future studies within this research project and be disseminated to non-academic audiences in this process. This will be completed through qualitative work involving focus groups involving policymakers, expectant mothers and charities. We plan to conduct evidence briefings as well as provide online resources.

PATIENT AND PUBLIC INVOLVEMENT

At this stage, there has been no patient or public involvement in the design, conduct or reporting of this research. We plan to involve the public in the dissemination planning for this research.

X Richard Fry @richfry

Acknowledgements In the scoping review, those within the second reviewer team who are not already mentioned in authorship will be acknowledged here, depending on their contribution to this review. We will also acknowledge the PPI groups who were involved in the dissemination planning of this research. This scoping review is the first study in a mixed-method thesis to investigate the impact of air pollution and birth outcomes. This review will inform further studies within this project.

Contributors LP is responsible for the overall content as guarantor. LP was involved with conceptualisation, methodology, investigation, writing (original draft) and writing (review and editing). AI, AM, KE-D and RF were involved with supervision and writing (review and editing). AI and AM also contributed to conceptualisation and methodology. KE-D was also involved with methodology and resources. All authors read and approved the final manuscript.

Funding This research was conducted as part of a fully funded studentship in the Faculty of Medicine, Health, and Life Science at Swansea University awarded to Lucy Perry with guidance from her supervisors.

Competing interests None declared.

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

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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