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Review article

Wildfire smoke exposure during pregnancy and perinatal, obstetric, and early childhood health outcomes: A systematic review and meta-analysis☆

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ABSTRACT

Background: Maternal exposure to air pollution during pregnancy is associated with adverse birth outcomes, although less is known for wildfire smoke. This systematic review evaluated the association between maternal exposure to wildfire smoke during pregnancy and the risk of perinatal, obstetric, and early childhood health outcomes.

Methods: We searched CINAHL Complete, Ovid/EMBASE, Ovid/MEDLINE, ProQuest, PubMed, Scopus, Web of Science, and Google Scholar to identify relevant epidemiological observational studies indexed through September 2023. The screening of titles, abstracts, and full-texts, data extraction, and risk of bias assessment was performed by pairs of independent reviewers.

Results: Our systematic search yielded 28,549 records. After duplicate removal, we screened 14,009 studies, identifying 31 for inclusion in the present review. Data extraction highlighted high methodological heterogeneity between studies, including a lack of geographic variation. Approximately 56.5% and 16% originated in the United States and Brazil, respectively, and fewer in other countries. Among the studies, wildfire smoke exposure during pregnancy was assessed using distance of residence from wildfire-affected areas ($n = 15$), measurement of air pollutant concentration during wildfires ($n = 11$), number of wildfire records ($n = 3$), aerosol index ($n = 1$), and geographic hot spots ($n = 1$). Pooled meta-analysis for birthweight and low birthweight were inconclusive, likely due to low number of methodologically homogenous studies. However, the reviewed studies provided suggestive evidence for an increased risk of birthweight reduction, low birthweight, preterm birth, and other adverse health outcomes.

Conclusions: This review identified 31 studies evaluating the impacts of maternal wildfire smoke exposure on maternal, infant, and child health. Although we found suggestive evidence of harm from exposure to wildfire smoke during pregnancy, more methodologically homogenous studies are required to enable future meta-analysis with greater statistical power to more accurately evaluate the association between maternal wildfire smoke and adverse birth outcomes and other health outcomes.

1. Introduction

Climate change has resulted in severe environmental degradation and is contributing to the increased frequency, duration, and intensity of a range of severe weather events worldwide (United Nations Environment Programme, 2022). In particular, in recent years some regions of the world experienced longer and more intense wildfire seasons – most notably the 2019–2020 Black Summer wildfires in Australia (Borchers Arriagada et al., 2020), the 2020 wildfires in the western United States (Li et al., 2021a), and the 2023 wildfires in Canada (Owens, 2023). Wildfires, whether started intentionally, accidently, or naturally, are unusual or extraordinary free-burning vegetation fires. In addition to devastation to wildlife, ecosystems, and the environment, wildfires can both directly and indirectly impact human health (United Nations

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Environment Programme, 2022). Direct exposure to wildfires can cause acute physical harm, such as burn-related injuries that may result in human mortality. Indirect wildfire exposure can lead to short- and long-term adverse health outcomes due to hazardous air pollutants generated during the combustion process, such as fine and coarse particulate matter ($PM_{2.5}$ and PM_{10}, respectively), carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and other toxic compounds (such as volatile organic compounds and polycyclic aromatic hydrocarbons [PAHs]) (United Nations Environment Programme, 2022; World Health Organization, 2021).

Short-term exposure to wildfire smoke is associated with increased hospital admissions, emergency department visits, and other wildfire smoke-related morbidities such as asthma, chronic obstructive pulmonary disease, ischemic heart disease, stroke, and other cardiovascular and respiratory complications (Gao et al., 2023; Elser et al., 2023; Wen et al., 2022; Borchers Arriagada et al., 2019). Pregnant women may be particularly vulnerable to health complications as a consequence of exposure to wildfire smoke, with respect to their own health as well as their offspring (Center for Disease Control and Prevention, 2021). Several chemical components commonly found in wildfire smoke, including heavy metals and PAHs, are known to accumulate in the placenta/fetus, and lead to developmental toxicity (Thangavel et al., 2022). Air pollutants, from wildfire smoke as well as other sources, may cross the blood-placental barrier, disrupt maternal-fetal blood circulation, and ultimately impact fetal development (Chen et al., 2021; Basilio et al., 2022).

A previous systematic review evaluated the association between exposure to wildfire smoke during pregnancy and adverse birth outcomes. This study found that exposure to wildfire smoke during pregnancy was significantly associated with reduced birthweight and preterm birth (Amjad et al., 2021). Despite these significant findings, the authors of the previous systematic review suggested that there is a limited body of evidence to confirm this association and that additional research is needed. Since the publication of the abovementioned systematic review, multiple studies have been published on the impacts of maternal wildfire smoke exposure. Therefore, the primary objective of this study was to synthesize the current evidence regarding the association between wildfire smoke exposure during pregnancy and adverse birth outcomes as well as to explore potential associations with other related adverse health outcomes (e.g., gestational diabetes). To our knowledge, this is the first systematic review on the longer-term impacts of wildfire smoke exposure during pregnancy beyond infancy and into early childhood and on the mother during pregnancy. This review aimed to expand on the current evidence by examining whether there was a differential effect of wildfire smoke exposure during pregnancy on health outcomes by trimester of exposure, which was not assessed in the earlier review.

2. Methods

We conducted a systematic review of the literature related to the impacts of wildfire smoke exposure during pregnancy on adverse health outcomes in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2022). Evidence-based reporting was guided by the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines (Page et al., 2021). A protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (registration number: CRD42022358861).

2.1. Data sources and search strategy

We searched for literature from database inception to September 11, 2022, in the following seven electronic databases: CINAHL Complete, Ovid/EMBASE, Ovid/MEDLINE, ProQuest, PubMed, Scopus, and Web of Science, using a combination of medical subject headings, keywords, and search terms related to the exposure and outcome. Additionally, we searched Google Scholar for gray literature (**S1 Table**). We also used backward and forward citation chaining (i.e., examining the reference lists of the included studies and subsequent studies that cited the included studies) to search for potentially relevant records not identified by the initial electronic search. The search strategy was developed in consultation with a research librarian (Higgins et al., 2022).

2.2. Eligibility criteria

Studies needed to satisfy five criteria to be eligible for inclusion: (1) study design criterion: epidemiological observational studies (e.g., cross-sectional, case-control, case-crossover, cohort, time-series, and ecological studies); (2) population criterion: pregnant women and/or their infants and young children; (3) exposure criterion: exposure to wildfire smoke during pregnancy; (4) outcome criterion: studies examining adverse health outcomes; and (5) effect estimate criterion: studies reporting quantitative measures of association (i.e., odds ratio [OR], relative risk [RR], hazard ratio [HR], regression coefficient) or net/percent change in the outcome (e.g., weight in grams) with 95% confidence intervals (CI) and/or *p*-values. We excluded studies not conducted on humans, case studies, case series, editorials, commentaries, letters, and reviews.

2.3. Study selection

All unique records identified from the electronic databases were imported into Covidence (Babineau, 2014). Each study was screened by two reviewers (among DF, RS, SH, GD, HMC, YS, and MLB) independently in two stages in accordance with the inclusion and exclusion criteria: 1) screening of titles and abstracts; and then 2) screening of the full-text articles. Studies deemed to meet the inclusion criteria by two reviewers were included in the final review. Any conflicts during each of the screening and reviewing stages were resolved through discussion by DF and GD.

2.4. Data extraction and risk of bias assessment

We developed a standardized data collection form to extract information on geographic location, study design, sample size, participant demographics, definition and ascertainment of exposure, outcome, and adjustment variables, effect sizes, and statistical uncertainty (e.g., confidence intervals and/or *p*-values). Information from each of the included studies was independently extracted by two reviewers. When information from the studies seemed to be imprecise or when results seemed available but was not provided in the article, the corresponding authors were contacted to request for additional information.

We evaluated the risk of bias of the included studies using the National Toxicology Program's Office of Health Assessment and Translation (OHAT) tool (National Institute of Environmental Health Sciences, 2019). The OHAT tool addresses five major bias domains: selection bias, confounding bias, exclusion/attrition bias, detection (exposure/outcome) bias, and selective reporting bias. In accordance with the OHAT tool scoring, studies were classified as having "high risk of bias", "probably high risk of bias", "probably low risk of bias", or "low risk of bias". Risk of bias was independently assessed by two reviewers. Any disagreements regarding the risk of bias scores were resolved through discussion by DF and RS and/or by a third reviewer.

2.5. Data synthesis

Due to high methodological heterogeneity between the included studies (i.e., different study designs, ascertainment and definition of exposure, evaluated outcomes, and analytical approach), we were unable to perform a meta-analysis for most outcomes. Instead, the findings were narratively described and summarized in text and tables. For studies that measured the concentration of wildfire smoke-related air

pollutants, we transformed the effect estimates to a standardized unit increment increase of the pollutant. For studies that only measured the PM_{10} concentration, the $PM_{2.5}$ concentration was estimated using a location-specific conversion factor ($PM_{2.5}$:PM_{10} ratio). The effect estimates for the included studies are presented in S2 Table.

2.6. Statistical analyses

All statistical analyses were performed using STATA version 15.1 (StataCorp LLC, College Station, Texas, U.S.). In this meta-analysis, we used the net change, ORs, RRs, and HRs and their corresponding 95% CIs as measures of association between wildfire smoke exposure and the outcomes for each study. For studies reporting effect estimates per unit increment of air pollutant concentration, we used the transformed effect estimates per standardized unit increment increase of the air pollutant (i.e., 5 μg/m^3). We also stratified the analyses by trimester of exposure. Due to different study designs, exposures, outcomes, and analytical approaches, heterogeneity was expected. Therefore, the DerSimonian and Laird random-effects model was selected to account for within- and between-study heterogeneity. We used the Hartung-Knapp-Sidik-Jonkman method, commonly used when the effect size is calculated from 20 or fewer effect sizes, to generate more robust results with more accurate error rates (Langan et al., 2019). The heterogeneity between studies was assessed using the Cochran's Q chi-square test and I_2 analysis (I_2 values of ≤25%, ≤50%, and ≤75% indicating low, moderate, and high heterogeneity, respectively) (Higgins et al., 2003). Publication bias was assessed quantitatively using Egger's test (Egger et al., 1997). $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Study selection

We identified 14,009 unique records, of which 13,915 were excluded after title and abstract screening. We reviewed 94 full-text articles, of which 31 studies were deemed eligible for inclusion (Fig. 1). The

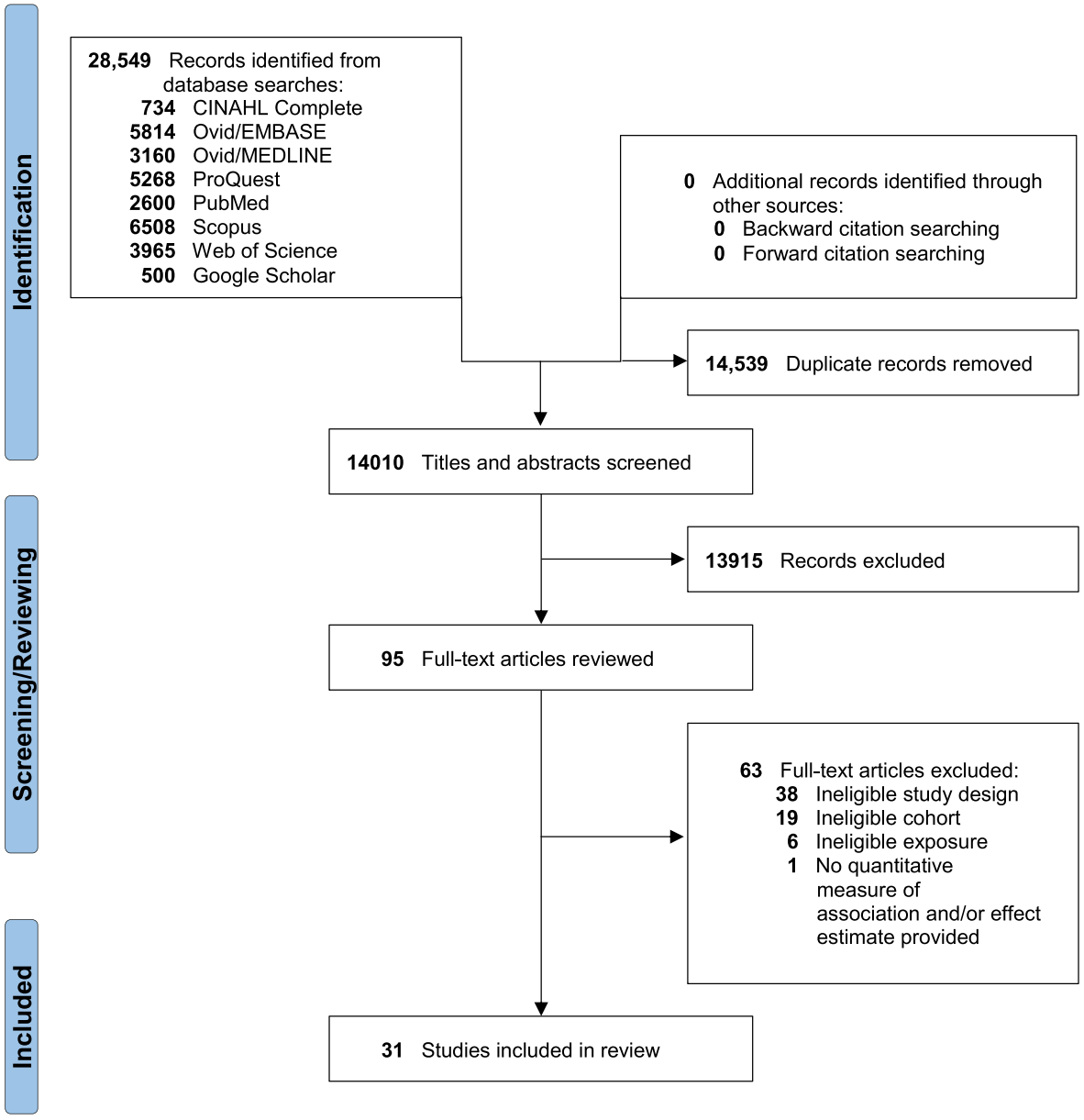

Fig. 1. Flow diagram of study selection process for systematic review of literature on the association between exposure to wildfire smoke during pregnancy and adverse perinatal, non-specific morbidity, and mortality outcomes.

primary reasons for exclusion included ineligible study design ($n = 38$), ineligible cohort ($n = 19$), ineligible exposure ($n = 6$), and no quantitative measure of association and/or effect estimate provided ($n = 1$).

3.2. Study characteristics

Of the 31 included studies, five were published as abstracts only and no corresponding full-text articles were identified (Waldrop et al., 2023; Kornfield et al., 2022; Nobles and Liu, 2021; Park et al., 2021; Breton et al., 2011). The 31 studies originated from the United States ($n = 13$) (Dhingra et al., 2023; Fernández et al., 2023; Waldrop et al., 2023; Heft-Neal et al., 2022; Jones and McDermott, 2022; Kornfield et al., 2022; Park et al., 2021, 2022; McCoy and Zhao, 2021; Nobles and Liu, 2021; Abdo et al., 2019; Holstius et al., 2012; Breton et al., 2011), Brazil ($n = 5$) (Requia et al., 2022a; Requia et al., 2022b; Requia et al., 2022c; da Silva et al., 2014; Prass et al., 2012), Australia ($n = 4$) (Zhang et al., 2023; Brew et al., 2022; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013), Indonesia ($n = 1$) (Jayachandran, 2009), South Korea ($n = 1$) (Jung et al., 2023), Thailand ($n = 1$) (Mueller et al., 2021), or were multi-country studies ($n = 6$) (Li et al., 2023; Pullabhotla et al., 2023; Xue et al., 2023; Li et al., 2022; Li et al., 2021b; Xue et al., 2021), with study periods ranging between 1996 and 2020. There were 19 birth cohort studies (Fernández et al., 2023; Jung et al., 2023; Waldrop et al., 2023; Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Kornfield et al., 2022; Park et al., 2022; Requia et al., 2022b; McCoy and Zhao, 2021; Nobles and Liu, 2021; Park et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; da Silva et al., 2014; O'Donnell and Behie, 2013; Holstius et al., 2012; Breton et al., 2011), six case-control studies (Pullabhotla et al., 2023; Xue et al., 2021, 2023; Li et al., 2021b, 2022; Requia et al., 2022a), two cross-sectional studies, (Li et al., 2023; Prass et al., 2012) and one study each for case-crossover (Requia et al., 2022c), cohort (Dhingra et al., 2023), ecological (Jayachandran, 2009), and semi-ecological (Mueller et al., 2021) designs. The study populations included infants ($n = 25$) (Fernández et al., 2023; Jung et al., 2023; Li et al., 2023; Pullabhotla et al., 2023; Waldrop et al., 2023; Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Li et al., 2022; Park et al., 2022; Requia et al., 2022a; Requia et al., 2022b; Requia et al., 2022c; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Park et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; da Silva et al., 2014; O'Donnell and Behie, 2013; Holstius et al., 2012; Prass et al., 2012; Breton et al., 2011), children ($n = 3$) (Dhingra et al., 2023; Li et al., 2022; Jayachandran, 2009), and pregnant women ($n = 6$) (Xue et al., 2023; Brew et al., 2022; Kornfield et al., 2022; Nobles and Liu, 2021; Xue et al., 2021; Abdo et al., 2019). Among the studies examining outcomes in infants, some restricted the study population to liveborn (Li et al., 2022; Requia et al., 2022b; Li et al., 2021b; Abdo et al., 2019; da Silva et al., 2014; Holstius et al., 2012; Prass et al., 2012), singleton (Fernández et al., 2023; Jung et al., 2023; Heft-Neal et al., 2022; Abdo et al., 2019; da Silva et al., 2014; Holstius et al., 2012), term (Jung et al., 2023; Requia et al., 2022a; Mueller et al., 2021; da Silva et al., 2014; Holstius et al., 2012), or preterm (Requia et al., 2022c) infants. The study characteristics of the included studies are presented in Table 1.

3.3. Risk of bias evaluation

We present the distribution of risk of bias of the included studies in Fig. 2. We did not exclude studies from this review based on the risk of bias results; studies published as abstracts were not assessed for risk of bias. The commonly identified potential source of bias among the included studies was confounding bias due to failure to account for key confounders including sociodemographic factors, such as maternal age ($n = 7$; 26.9%), race/ethnicity ($n = 18$; 69.2%), education ($n = 15$; 57.7%), and/or socioeconomic status ($n = 22$; 84.6%) (S3 Table). Other identified potential sources of bias include detection bias of the exposure and outcome, and selection bias. Exclusion/attrition and selective reporting bias were less common among the included studies.

3.4. Exposure assessment

The included studies employed various methods to evaluate exposure to wildfire smoke during pregnancy. Most studies used proxy measures of wildfire smoke exposure, including spatial overlap of maternal residence with wildfire-affected areas ($n = 15$) (Dhingra et al., 2023; Jung et al., 2023; Waldrop et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Kornfield et al., 2022; Park et al., 2022; McCoy and Zhao, 2021; Nobles and Liu, 2021; Park et al., 2021; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013; Holstius et al., 2012; Breton et al., 2011), the number of wildfire records (provided by the National Institute of Spatial Research of Brazil; $n = 3$) (Requia et al., 2022a,b,c), the Total Ozone Mapping Spectrometer aerosol index ($n = 1$) (Jayachandran, 2009), and geographic heat spots ($n = 1$) (Prass et al., 2012). Nine studies used measurements of the concentration of wildfire smoke-related air pollutants ($PM_{2.5}$ [$n = 11$] (Fernández et al., 2023; Li et al., 2023; Xue et al., 2023; Zhang et al., 2023; Heft-Neal et al., 2022; Li et al., 2022; Requia et al., 2022c; Li et al., 2021b; Xue et al., 2021; Abdo et al., 2019; da Silva et al., 2014), PM_{10} [$n = 1$] (Mueller et al., 2021), and CO [$n = 1$] (da Silva et al., 2014)), of which only one used monitored data (Mueller et al., 2021). For a study conducted in Thailand (Mueller et al., 2021) that reported results per unit increment of wildfire smoke-related PM_{10} concentration, we calculated the $PM_{2.5}$ concentration from the PM_{10} concentration in accordance with conversion factor (0.63 $\mu g/m^3$ $PM_{2.5}$: 1 $\mu g/m^3$ PM_{10}) specific to Thailand. Two studies used measurements of the burned area (Pullabhotla et al., 2023; Mueller et al., 2021). Comparisons were made between wildfire-affected areas with areas not exposed (Fernández et al., 2023; Jones and McDermott, 2022; Park et al., 2022; Requia et al., 2022c; McCoy and Zhao, 2021; Nobles and Liu, 2021; Park et al., 2021; O'Donnell and Behie, 2013; Breton et al., 2011) or less exposed (O'Donnell and Behie, 2015) to wildfire, between wildfire-affected cohorts and cohorts unaffected by wildfire during different timeframes (Jung et al., 2023; Brew et al., 2022; Kornfield et al., 2022; O'Donnell and Behie, 2013; Holstius et al., 2012; Jayachandran, 2009), or by incremental increased exposure to wildfire smoke (Dhingra et al., 2023; Fernández et al., 2023; Li et al., 2023; Pullabhotla et al., 2023; Waldrop et al., 2023; Xue et al., 2023; Zhang et al., 2023; Heft-Neal et al., 2022; Li et al., 2022; Requia et al., 2022a; Requia et al., 2022b; Requia et al., 2022c; Li et al., 2021b; Mueller et al., 2021; Xue et al., 2021; Abdo et al., 2019; da Silva et al., 2014; Prass et al., 2012).

3.5. Outcome assessment

The most frequently examined outcomes included birthweight ($n = 16$) (Fernández et al., 2023; Jung et al., 2023; Li et al., 2023; Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Li et al., 2022; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013; Holstius et al., 2012; Prass et al., 2012; Breton et al., 2011), low birthweight ($n = 9$), (Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Requia et al., 2022a; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; da Silva et al., 2014) and preterm birth ($n = 8$) (Waldrop et al., 2023; Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Requia et al., 2022c; Abdo et al., 2019; Breton et al., 2011). Other studied outcomes included gestational length ($n = 3$), (Jones and McDermott, 2022; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013) small-for-gestational age ($n = 4$), (Fernández et al., 2023; Brew et al., 2022; Abdo et al., 2019; Breton et al., 2011) gestational diabetes mellitus ($n = 2$), (Brew et al., 2022; Abdo et al., 2019) gestational hypertension ($n = 2$), (Brew et al., 2022; Abdo et al., 2019) stillbirth ($n = 2$) (Xue et al., 2023; Brew et al., 2022), and other outcomes ($n = 1$). Most studies ascertained the outcome(s) of interest using birth certificate

Table 1
Characteristics of included studies ($n = 31$).

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information

Dhingra et al. (2023)
 	
Six states: California, Idaho, Montana, Nevada, Oregon, and Washington (United States)
 	
Cohort study
	2010–2016	$N = 113{,}154$ children	*Method of exposure ascertainment:*
			• Satellite imaging
			Spatial resolution of exposure:
			• Metropolitan statistical area-level
			Exposure:
			• Exposure to wildfire smoke during pregnancy by trimester:
			  • 1st trimester
			  • 2nd trimester
			  • 3rd trimester
			Comparison:
			• Lower number of days of wildfire smoke exposure during pregnancy
				Method of outcome ascertainment:
				• Prescription claim records
				Outcomes:
				• Prescription claim of:
				  • Lower respiratory infection medication
				  • Systematic anti-inflammatory medication
				  • Upper respiratory infection medication

Fernández (2023) San Francisco (United States) Birth cohort study	1 January 2017 –12 March 2020	$N = 7923$ infants	*Method of exposure ascertainment:* • Ensemble-based modelling developed using machine learning algorithms *Spatial resolution of exposure:* • ZIP code-level *Exposure:* • Exposure to wildfire smoke during pregnancy by trimester: • Any trimester • 1st trimester • 2nd trimester • 3rd trimester *Comparison:* • No wildfire smoke exposure during pregnancy • Lower number of days of wildfire smoke exposure during pregnancy	*Method of outcome ascertainment:* • Birth records *Outcomes:* • Birthweight • Large-for-gestational age • Small-for-gestational age
Jung et al. (2023) Yeongdong region (South Korea) Birth cohort study	1 January 1999–31 December 2001	$N = 6921$ infants	*Method of exposure ascertainment:* • Dates of wildfire *Spatial resolution of exposure:* • ZIP code-level *Exposure groups:* • Exposure to wildfire smoke during pregnancy by trimester: • Any trimester • 1st trimester • 2nd trimester • 3rd trimester *Comparison groups:* • No wildfire smoke exposure during pregnancy	*Method of outcome ascertainment:* • Birth records *Outcome:* • Birthweight (g)
Li et al. (2023) 17 low- and middle-income countries Cross-sectional study	16 September 2017–15 September 2018	$N = 53{,}449$ infants	*Method of exposure ascertainment:* • Chemical transport and satellite remote sensing modelling *Spatial resolution of exposure:* • $0.01^\circ \times 0.01^\circ$ grid-level (~1 km × 1 km) *Exposure*:	*Method of outcome ascertainment:* • Demographic and Health Surveys (health card or self-reported by mothers) *Outcome:* • Birthweight (g)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
			• Exposure to open fire smoke-related $PM_{2.5}$ during pregnancy *Comparison*: • Lower concentration of open-fire smoke $PM_{2.5}$ exposure during pregnancy	
Pullabhotla et al. (2023) 54 low- and middle-income countries Case-control study	2004–2018	$N = 2{,}237{,}307$ infants	*Method of exposure ascertainment:* • Burned area data using satellite imaging from the European Space Agency Climate Change Initiative *Spatial resolution of exposure:* • $0.05^\circ \times 0.05^\circ$ grid-level (~5 km × 5 km) *Exposure:* • Exposure to biomass burning during pregnancy *Comparison*: • Lower concentration of biomass burning exposure during pregnancy	*Method of outcome ascertainment:* • Demographic and Health Surveys (self-reported by mothers) *Outcome:* • Infant mortality (<1 year)
Waldrop et al. (2023) California (United States) Birth cohort study	2007–2012	$N = 2{,}548{,}347$ pregnant women and infants	*Method of exposure ascertainment:* • Satellite-based modelling *Spatial resolution of exposure:* • High-resolution grid-level (not specified in abstract) *Exposure:* • Exposure to wildfire smoke during pregnancy by exposure window: • 4 weeks pre-conception to week 20 gestational age • 4 weeks pre-conception to birth • 1st trimester • Week 14–20 gestational age *Comparison:* • Lower number of days of wildfire smoke exposure during pregnancy	*Method of outcome ascertainment:* • Birth certificate and hospital records *Outcomes:* • Hypertensive disorders during pregnancy • Preterm birth (<37 weeks gestation)
Xue et al. (2023) 54 low- and middle-income countries Case-control study	2000–2014	$N = 35{,}590$ pregnant women	*Method of exposure ascertainment:* • 3-D Term low birthweight chemical transport (GEOS-Chem) model *Spatial resolution of exposure:* • $0.01^\circ \times 0.01^\circ$ grid-level (~1 km × 1 km) *Exposure:* • Exposure to wildfire smoke exposure during pregnancy *Comparison:* • Lower concentration of wildfire smoke exposure during pregnancy	*Method of outcome ascertainment:* • Demographic and Health Surveys (self-reported by mothers) *Outcomes:* • Stillbirth
Zhang et al. (2023) New South Wales (Australia) Birth cohort study	2015–2019	$N = 330{,}884$ infants	*Method of exposure ascertainment:* • 3-D chemical transport (GEOS-Chem) model, machine learning, and remote-sensing data *Spatial resolution of exposure:* • $0.25^\circ \times 0.25^\circ$ grid-level (~25 km × 25 km)	*Method of outcome ascertainment:* • Birth records *Outcomes:* • Birthweight (g) • Low birthweight (<2500 g)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information

			Exposure:
			• Exposure to wildfire smoke exposure during pregnancy
			Comparison:
			• Lower concentration of wildfire smoke exposure during pregnancy
				• Term low birthweight (<2500 g)
				• Preterm birth (<37 weeks gestation)
				  • Very preterm birth (<32 weeks gestation)
				  • Late preterm birth (32–37 weeks gestation)

Brew et al. (2022)
South Sydney (Australia)
Birth cohort study
	November 2017–December 2020	$N = 60{,}054$ pregnant women and infants	*Method of exposure ascertainment*:
			• Air monitoring data from the Climate and Atmospheric Science Branch, Department of Planning Industry and Environment of New South Wales Government
			Spatial resolution of exposure:
			• Local health district-level
			Exposure groups:
			• Wildfire smoke exposure during pregnancy
			• Wildfire smoke exposure during pregnancy and COVID-19 pandemic lockdown 1
			• Wildfire smoke exposure during pregnancy and COVID-19 pandemic lockdown 2
			Comparison group:
			• Historical cohort of previous years unexposed to wildfire smoke during pregnancy
				Method of outcome ascertainment:
				• Birth records
				Outcomes:
				• Gestational diabetes mellitus
				• Gestational hypertension (including chronic hypertension, gestational hypertension, and pre-eclampsia)
				• High birthweight (>4000 g)
				• Low birthweight (<2500 g)
				• Mode of birth:
				  • Unplanned cesarean section
				  • Planned cesarean section
				  • Induction of labor
				• Pre-eclampsia
				• Pre-labor rupture of membranes
				• Preterm birth (<37 weeks gestation)
				• Small-for-gestational age
				• Stillbirth

Heft-Neal et al. (2022)
California (United States)
Birth cohort study
	2006–2012	$N = 3{,}063{,}672$ infants	*Method of exposure ascertainment*:
			• NOAA satellite imaging and the ensemble-based modelling developed using machine learning algorithms
			Spatial resolution of exposure:
			• ZIP code-level
			Exposures:
			• Exposure to wildfire smoke during pregnancy by trimester:
			  • Any trimester
			  • 1st trimester
			  • 2nd trimester
			  • 3rd trimester
			Comparison:
			• Lower number of days of wildfire smoke exposure during pregnancy
				Method of outcome ascertainment:
				• Birth records
				Outcomes:
				• Preterm birth (<37 weeks gestation)
				• Very preterm birth (<32 weeks gestation)
				• Extremely preterm birth (<28 weeks gestation)

Jones and McDermott (2022) 85 counties across 17 states (United States) Birth cohort study	2010–2017	$N = 689{,}762$–$689{,}997$ infants	*Method of exposure ascertainment*: • USGS Geospatial Multi-Agency Coordination (GeoMAC) system *Spatial resolution of exposure:* • County-level *Exposure group*: • Megafire smoke exposure during pregnancy *Comparison group*: • No megafire smoke exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Birthweight (g) • Gestational length (weeks) • Low birthweight (<2500 g) • Preterm birth (<37 weeks gestation)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
Kornfield et al. (2022) Oregon (United States) Birth cohort study (abstract)	20 August 2019–31 October 2020	$N = 248$ pregnant women	*Method of exposure ascertainment*: • Not specified in abstract *Spatial resolution of exposure:* • Not specified in abstract *Exposure group*: • Wildfire smoke exposure during pregnancy *Comparison group*: • Historical cohort of previous year unexposed to wildfire smoke during pregnancy	*Method of outcome ascertainment*: • Self-reported by mother *Outcomes*: • Pregnancy loss (including miscarriage and stillbirth) • Gestational duration between exposure and pregnancy loss
Li et al. (2022) 54 low- and middle-income countries Case-control study	2000–2014	$N = 228{,}661$ infants and children born to 109,466 mothers	*Method of exposure ascertainment*: • 3-D chemical transport (GEOS-Chem) model *Spatial resolution of exposure:* • $0.05^\circ \times 0.05^\circ$ grid-level (~5 km × 5 km) *Exposure*: • Exposure to landscape fire smoke-related $PM_{2.5}$ during pregnancy *Comparison*: • Lower concentration of landscape fire smoke-related $PM_{2.5}$ exposure during pregnancy	*Method of outcome ascertainment*: • Demographic and Health Surveys (self-reported by mothers) *Outcomes*: • Birthweight (g) • Under-5 child mortality

Park et al. (2022)
California (United States)
Birth cohort study
	2007–2010	$N = 2{,}093{,}185$ infants	*Method of exposure ascertainment*:
			• Wildfire records from the California Department of Forestry and Fire Protection
			Spatial resolution of exposure:
			• ZIP code-level
			Exposure groups:
			• Pre-pregnancy exposure to wildfire smoke (within 30 days of conception)
			• Wildfire smoke exposure during pregnancy by:
			  • Trimester:
			  • 1st trimester
			  • 2nd trimester
			  • 3rd trimester
			Comparison group:
			• No wildfire smoke exposure during pregnancy
				Method of outcome ascertainment:
				• Birth records
				Outcome:
				• Fetal gastroschisis

Requia et al. (2022a) Brazil Case-control study	2001–2018	$N = 1{,}602{,}471$ term infants	*Method of exposure ascertainment*: • Satellite imaging *Spatial resolution of exposure:* • Municipality-level *Exposures*: • Exposure to wildfire smoke during pregnancy (number of wildfire records per municipality/day) by trimester: • 1st trimester • 2nd trimester • 3rd trimester	*Method of outcome ascertainment*: • Birth records *Outcome*: • Low birthweight (<2500 g)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
			Comparison: • Lower wildfire smoke exposure during pregnancy (lower number of wildfire records per municipality/day)	

Requia et al. (2022b)
Brazil
Birth cohort study
	2001–2018	$N = 16{,}825{,}497$ term infants	*Method of exposure ascertainment*:
			• Satellite imaging
			Spatial resolution of exposure:
			• Municipality-level
			Exposures:
			• Incremental increased exposure to wildfire smoke during pregnancy (number of wildfire records per municipality/day) by:
			  • Trimester:
			  • 1st trimester
			  • 2nd trimester
			  • 3rd trimester
			Comparison:
			• Lower wildfire smoke exposure during pregnancy (lower number of wildfire records per municipality/day)
				Method of outcome ascertainment:
				• Birth records
				Outcomes:
				• Chromosomal anomalies
				• Congenital anomalies of the:
				  • Circulatory system
				  • Digestive system
				  • Eyes, ears, face, and neck
				  • Musculoskeletal system
				  • Genital organs
				  • Nervous system
				  • Respiratory system
				  • Urinary system
				• Other congenital anomalies
				• Cleft lip and cleft palate
				• Benign neoplasms/tumors

Requia et al. (2022c) Brazil Case-crossover study	2001–2018	$N = 190{,}911$ preterm infants	*Method of exposure ascertainment*: • Satellite imaging *Spatial resolution of exposure:* • Municipality-level *Exposure groups*: • Exposure to wildfire smoke during pregnancy (number of wildfire records and mean $PM_{2.5}$ concentration per municipality/day) by trimester: • 1st trimester • 2nd trimester • 3rd trimester *Comparison group*: • Unexposed trimesters to wildfire smoke	*Method of outcome ascertainment*: • Birth records *Outcome*: • Preterm birth (<37 weeks gestation)
Li et al. (2021b) 54 low- and middle-income countries Case-control study	2000–2014	$N = 227{,}948$ infants born to 109,137 mothers	*Method of exposure ascertainment*: • 3-D chemical transport (GEOS-Chem) model *Spatial resolution of exposure:* • Spatial overlap between the wildfire smoke plume boundaries and coordinates of the mother's residential address *Exposure*: • Exposure to landscape fire smoke-related $PM_{2.5}$ during pregnancy *Comparison*: • Lower concentration of landscape fire smoke-related $PM_{2.5}$ exposure during pregnancy	*Method of outcome ascertainment*: • Demographic and Health Surveys (self-reported by mothers) *Outcomes*: • Birthweight (g) • Low birthweight (<2,500 g) • Very low birthweight (not specified in manuscript)
McCoy and Zhao (2021) Colorado (United States) Birth cohort study	2007–2013	$N = 158{,}906$ infants	*Method of exposure ascertainment*: • Geographic information system using daily satellite imaging *Spatial resolution of exposure:*	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Low birthweight (<2,500 g)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
			• Coordinates of the mother's residential address *Exposure group*: • Wildfire smoke exposure during pregnancy *Comparison group*: • No wildfire smoke exposure during pregnancy	• Birthweight (%)
Mueller et al. (2021) Seven provinces: Chon Buri, Rayong, Lampang, Phrae, Nan, Phayao, Nakhon Sawan (Thailand) Semi-ecological study	2015–2018	$N = 83{,}931$ term infants	*Method of exposure ascertainment*: • Ground-based PM_{10} monitoring *Spatial resolution of exposure:* • Province-level *Exposures*: • Exposure to biomass burning-related PM_{10} during pregnancy • Exposure to biomass burning during pregnancy *Comparisons*: • Lower concentration of biomass burning-related PM_{10} exposure during pregnancy • Lower concentration of biomass burning exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Birthweight (g) • Low birthweight (<2,500 g)
Nobles and Liu (2021) California (United States) Birth cohort study (abstract)	2014–2016	$N = >11{,}000$ pregnant women	*Method of exposure ascertainment*: • Not specified in abstract *Spatial resolution of exposure:* • Not specified in abstract *Exposure groups*: • Pre-pregnancy exposure to wildfire smoke • Wildfire smoke exposure during first trimester *Comparison group*: • No wildfire smoke exposure during pregnancy	*Method of outcome ascertainment*: • Not specified in abstract *Outcome*: • First trimester pregnancy loss
Park et al. (2021) California (United States) Birth cohort study (abstract)	2007–2010	$N = 1{,}904{,}344$ infants	*Method of exposure ascertainment*: • Wildfire records from the California Department of Forestry and Fire Protection *Spatial resolution of exposure:* • ZIP code-level *Exposure groups*: • Pre-pregnancy exposure to wildfire smoke (within 30 days of conception) • Wildfire smoke exposure during pregnancy *Comparison group*: • No wildfire smoke exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcome*: • Spina bifida
Xue et al. (2021) India, Pakistan, and Bangladesh Case-control study	2000–2014	$N = 75{,}262$ pregnancies of 24,876 pregnant women	*Method of exposure ascertainment*: • MODIS satellite imaging, fire emission database, and 3-D chemical transport (GEOS-Chem) model	*Method of outcome ascertainment*: • Demographic and Health Surveys (self-reported by mothers)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
			Spatial resolution of exposure: • 0.1° × 0.1° grid-level (~10 km × 10 km) • 0.25° × 0.25° grid-level (~25 km × 25 km) • 0.5° × 0.625° grid-level (~50 km × 62.5 km) *Exposure*: • Exposure to open fire smoke-related $PM_{2.5}$ during pregnancy *Comparison*: • Lower concentration of open-fire smoke $PM_{2.5}$ exposure during pregnancy	*Outcome*: • Pregnancy loss (i.e., spontaneous abortion, induced abortion, or stillbirth)
Abdo et al. (2019) Colorado (United States) Birth cohort study	2007–2015	534,798 pregnant women and infants	*Method of exposure ascertainment*: • NOAA satellite imaging *Spatial resolution of exposure:* • 15 km × 15 km-matched ZIP code-level *Exposure*: • Exposure to wildfire smoke-related $PM_{2.5}$ during pregnancy *Comparison*: • Lower concentration of wildfire smoke-related $PM_{2.5}$ exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Assisted ventilation following delivery • Birthweight (g) • Gestational diabetes mellitus • Gestational hypertension • Neonatal intensive care unit admission • Low birthweight (<2500 g) • Preterm birth (<37 weeks gestation) • Small-for-gestational age
O'Donnell and Behie (2015) Canberra (Australia) Birth cohort study	2000–2010	$N = 48{,}408$ infants	*Method of exposure ascertainment*: • Self-reported location of residence at birth *Spatial resolution of exposure:* • Statistical Local Area-level *Exposure groups*: • High exposure to wildfire smoke during pregnancy (areas "severely affected" by wildfire; areas where both deaths and property damage occurred) • Moderate exposure to wildfire smoke during pregnancy (areas "moderately affected" by wildfire; areas where only property damage occurred) *Comparison group*: • Lower (moderate or low) exposure to wildfire smoke during pregnancy (areas "moderately affected" or "least affected" by wildfire; areas where no fire damage occurred)	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Birthweight (g) • Gestational length (weeks)
da Silva et al. (2014) Mato Grosso (Brazil) Birth cohort study	July 2004–December 2005	$N = 6147$ term infants	*Method of exposure ascertainment*: • CATT-BRAMS model *Spatial resolution of exposure:* • Municipality-level *Exposure groups*: • Higher quartiles (Q2, Q3, and Q4) of biomass burning-related $PM_{2.5}$ exposure during pregnancy • Higher quartiles (Q2, Q3, and Q4) of biomass burning-related CO exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcome*: • Low birthweight (<2500 g)

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information
			Comparison groups: • Lowest quartile (Q1) of daily biomass burning-related $PM_{2.5}$ exposure during pregnancy • Lowest quartile (Q1) of daily biomass burning-related CO exposure during pregnancy	
O'Donnell and Behie (2013) Victoria (Australia) Birth cohort study	2006–2009	$N = 287,688$ infants	*Method of exposure ascertainment*: • Reports from the Victoria Bushfires Royal Commission *Spatial resolution of exposure:* • Local Government Area-level *Exposure group*: • Wildfire smoke exposure during pregnancy (wildfire-affected area) *Comparison group*: • No wildfire smoke exposure during pregnancy (wildfire-unaffected areas or wildfire-affected areas during the same months in previous years)	*Method of outcome ascertainment*: • Birth records *Outcomes*: • Birthweight (g) • Gestational length (weeks) • Low birthweight • Sex ratio
Holstius et al. (2012) Southern California (United States) Birth cohort study	2001–2005	$N = 886,034$ infants	*Method of exposure ascertainment*: • Wildfire records from the California Department of Forestry and Fire Protection and MODIS satellite imaging *Spatial resolution of exposure:* • Census tract-level *Exposure groups*: • Exposure to wildfire smoke during pregnancy by trimester: • Any trimester • 1st trimester • 2nd trimester • 3rd trimester *Comparison group*: • No wildfire smoke exposure during pregnancy	*Method of outcome ascertainment*: • Birth records *Outcome*: • Birthweight (g)
Prass et al. (2012) Porto Velho (Brazil) Cross-sectional study	2001–2006	$N = 22,012$ infants	*Method of exposure ascertainment*: • NOAA satellite imaging *Spatial resolution of exposure:* • Not specified in manuscript *Exposure group*: • Wildfire smoke exposure during pregnancy (i.e., time period with higher number of heat spots) *Comparison group*: • Lower exposure to wildfire smoke during pregnancy (i.e., time period with lower number of heat spots)	*Method of outcome ascertainment*: • Birth records *Outcome*: • Birthweight (g)
Breton et al. (2011) Southern California (United States)	2003–2004	Infants Sample size not specified in abstract	*Method of exposure ascertainment*: • Not specified in abstract	*Method of outcome ascertainment*: • Birth records

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Table 1 (*continued*)

First author (y), setting, and study design	Study period	Sample size and study population	Exposure information	Outcome information

Birth cohort study (abstract)			*Spatial resolution of exposure:*
			• ZIP code-level
			Exposure groups:
			• Wildfire smoke-related $PM_{2.5}$ exposure during pregnancy
			  • Low exposure
			  • Medium exposure
			  • High exposure
			Comparison group:
			• No wildfire smoke-related $PM_{2.5}$ exposure during pregnancy
				Outcomes:
				• Birthweight (g)
				• Preterm birth (<37 weeks gestation)
				• Small-for-gestational age

Jayachandran (2009) Sumatra (Indonesia) Ecological study	December 1996–May 1998	N ≈ 1,300,000 children (calculated; not specified in manuscript)	*Method of exposure ascertainment*: • Earth Probe Total Ozone Mapping Spectrometer (TOMS) aerosol index *Spatial resolution of exposure:* • Subdistrict-level *Exposure group*: • Wildfire smoke exposure during pregnancy *Comparison group*: • No wildfire smoke exposure during pregnancy (children conceived before or after wildfire events)	*Method of outcome ascertainment*: • Inferred early-life mortality measured by "missing children" *Outcome*: • Under-3 early (fetal, infant, and child) mortality

records (n = 19) (Fernández et al., 2023; Jung et al., 2023; Waldrop et al., 2023; Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Park et al., 2022; Requia et al., 2022a; Requia et al., 2022b; Requia et al., 2022c; McCoy and Zhao, 2021; Mueller et al., 2021; Park et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; da Silva et al., 2014; O'Donnell and Behie, 2013; Holstius et al., 2012; Breton et al., 2011), while others used demographic and health survey data (n = 6) (Li et al., 2021b, 2022, 2023; Pullabhotla et al., 2023; Xue et al., 2021, 2023), hospital records (n = 2) (Waldrop et al., 2023; Prass et al., 2012), prescription claim records (n = 1) (Dhingra et al., 2023), were self-reported by the mother (n = 1) (Kornfield et al., 2022), or were inferred from Census data (n = 1) (Jayachandran, 2009) (Table 2).

3.6. Perinatal outcomes

3.6.1. Birthweight and low birthweight

3.6.1.1. Birthweight. Thirteen studies evaluated the associations between wildfire smoke exposure during pregnancy and birthweight, (Fernández et al., 2023; Jung et al., 2023; Li et al., 2023; Zhang et al., 2023; Jones and McDermott, 2022; Li et al., 2022; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013; Holstius et al., 2012; Prass et al., 2012) observing that higher exposure to wildfire smoke was associated with lower birthweight (−10.83 g to −48.68 g per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure (Zhang et al., 2023; Li et al., 2022; Li et al., 2021b; Mueller et al., 2021); −42.27 g per 1 fire/km^2 increase; (Mueller et al., 2021) and −6.1 g to −32.5 g, (Jung et al., 2023; Jones and McDermott, 2022; Holstius et al., 2012) and −3.88% (McCoy and Zhao, 2021) following wildfire smoke exposure during pregnancy overall compared to those unexposed to wildfire smoke during pregnancy; all statistically significant) (S2 Table). The trimester of exposure was considered in eight studies (Fernández et al., 2023; Jung et al., 2023; Zhang et al., 2023; Jones and McDermott, 2022; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; Holstius et al., 2012). Five studies observed a more pronounced reduction in birthweight following exposure to wildfire smoke in the earlier trimesters (Jung et al., 2023; Zhang et al., 2023; Jones and McDermott, 2022; McCoy and Zhao, 2021; Abdo et al., 2019) while one study reported a more pronounced reduction in birthweight in the later trimesters (Holstius et al., 2012). Two studies stratified by sex, of which the study in Thailand observed similar results between male and female infants (Mueller et al., 2021), and the other study in the United States observed an increase in the birthweight-for-gestational age z-score of 0.23 per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure (95% CI, 0.06 to 0.34) among female infants only (Fernández et al., 2023). Jones and McDermott (2022) reported a more pronounced and nonlinear reduction in birthweight following exposure to larger wildfires during pregnancy compared to infants of mothers unexposed to wildfire smoke during pregnancy (range: −4.83 g to −43.36 g; $p < 0.05$). In contrast, an Australian study by O'Donnell and Behie (2015) found a positive association between wildfire smoke exposure during pregnancy and birthweight. This study reported that infants of mothers residing in areas heavily affected by wildfire weighed 47–197 g more than infants of mothers residing in areas moderately affected ($p < 0.05$). However, this study also observed a 56 g reduction in birthweight among male infants of mothers residing in areas heavily affected by wildfires compared to male infants of mothers residing in areas moderately affected by wildfires in 2010 ($p = 0.03$).

3.6.1.2. Low birthweight. The association between wildfire smoke

Fig. 2. Distribution of Risk of Bias of included studies by Risk of Bias Domain using the National Toxicology Program's Office of Health Assessment and Translation tool.

exposure during pregnancy and low birthweight was evaluated in ten studies (Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Requia et al., 2022a; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; da Silva et al., 2014; O'Donnell and Behie, 2013) (S2 Table). The trimester of exposure was considered in nine studies (Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Requia et al., 2022a; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; da Silva et al., 2014; O'Donnell and Behie, 2013). Nine of the ten studies reported an association between wildfire smoke exposure during pregnancy and low birthweight. However, the effect direction differed within and between studies. Five studies reported consistent positive associations between wildfire smoke exposure during pregnancy and low birthweight, meaning higher exposure was associated with higher risk of low birthweight. The most recent study by Zhang et al. (2023) observed a 45% increased risk of low birthweight per 5 $\mu g/m^3$ increase in wildfire smoke-related $PM_{2.5}$ exposure (95% CI, 1.36 to 1.55). The increased risk was particularly higher for exposure during trimester 2 (aHR, 2.67; 95% CI, 2.42 to 2.93) compared to trimesters 1 and 3 (aHR, 1.73; 95% CI, 1.56 to 1.91 and aHR, 1.20; 95% CI, 1.15 to 1.25, respectively). In a sensitivity analysis restricted to term children, this study also observed a 4% increased risk of low birthweight per 5 $\mu g/m^3$ increase in wildfire smoke-related $PM_{2.5}$ exposure (95% CI, 1.02 to 1.07). The risk was greater among male infants (aHR, 1.32; 95% CI, 1.07 to 1.62), infants conceived during autumn and spring (aHR, 1.45; 95% CI, 1.24 to 1.70 and aHR, 24.38; 95% CI, 10.20 to 57.95, respectively), infants of mothers residing in inner regions of New South Wales, Australia (aHR, 1.61; 95% CI, 1.30 to 1.98), and infants exposed to wildfire smoke during trimesters 1 and 2 (aHR, 1.56; 95% CI, 1.29 to 1.86 and aHR, 1.39; 95% CI, 1.14 to 1.69, respectively). Similarly, positive associations were observed by Li et al. (2021b) (14.81% per 5 $\mu g/m^3$ increase in wildfire smoke-related $PM_{2.5}$ exposure; 95% CI, 4.95% to 25.58%) and Jones and McDermott (2022) (0.8%; $p < 0.01$). The former study was the only one that explored very low birthweight as an outcome and reported a 73.73% increased risk per 5 $\mu g/m^3$ increase in wildfire smoke-related $PM_{2.5}$ exposure (95% CI, 19.29% to 153.01%). The size of the wildfire and exposure during the earlier trimesters also led to pronounced positive associations in the latter study (range: 0.1% to 1.3%; $p < 0.05$) (Jones and McDermott, 2022).

O'Donnell and Behie (2013) reported a higher proportion of infants with low birthweights among those of mothers exposed to wildfire smoke during trimesters 1 and 3 (6.3% vs. 6.5% and 6.5% vs. 7.0%, respectively; $p < 0.05$) compared to infants of mothers residing in areas unaffected by wildfire. This study also observed a significant difference between the birthweights of infants of exposed mothers compared to infants of mothers unexposed to wildfire in the previous year, irrespective of the trimester of exposure ($p < 0.006$). One study by da Silva et al. (2014) considered wildfire smoke-related $PM_{2.5}$ and CO exposure during pregnancy using quartiles and stratified by trimester of exposure. Compared to quartile 1 exposure, quartile 4 exposure resulted in a significant increase in the odds of low birthweight following exposure to wildfire smoke-related $PM_{2.5}$ (trimester 2: aOR, 1.51; 95% CI, 1.04 to 2.17; trimester 3: aOR, 1.50; 95% CI, 1.06 to 2.15) and CO (trimester 2: aOR, 1.49; 95% CI, 1.03 to 2.14) during pregnancy.

Four studies reported inconsistent results. Mueller et al. (2021) evaluated wildfire smoke exposure using two different methods and found conflicting findings. This study observed a reduction in the odds of low birthweight following exposure to wildfire smoke during trimesters 1 and 2 (aOR, 0.96; 95% CI, 0.93 to 0.99 and aOR, 0.95; 95% CI, 0.92 to 0.98, respectively) per 5 $\mu g/m^3$ increase in wildfire smoke-related $PM_{2.5}$ exposure. Conversely, a significant increase in the odds of low birthweight was reported among male infants of mothers exposed to wildfire smoke during trimester 3 (aOR, 2.17; 95% CI, 1.13 to 4.12) per 1 fire/km^2 increase. Brew et al. (2022) reported a higher odds of low birthweight following exposure to wildfire smoke during pregnancy in conjunction with the COVID-19 pandemic lockdown 1 (aOR, 1.18; 95% CI, 1.03 to 1.37). However, when examining exposure to wildfire smoke alone during pregnancy, this study reported a negative association (aOR, 0.81; 95% CI, 0.69 to 0.95). A Brazilian study by Requia et al. (2022a) performed a series of stratifications by region, trimester of exposure, sex, and race/ethnicity, and mostly observed a positive association between wildfire smoke exposure during pregnancy and low birthweight. The study reported that for every 10 wildfire record increase per

Table 2
Summary of findings.

Outcome	Number of participants (number of studies)	Effect and effect direction[a]	
Perinatal health outcomes			
Assisted ventilation following delivery	$N = 534,798$ ($n = 1$) (Abdo et al., 2019)	The study observed an inverse association between exposure to wildfire smoke during pregnancy and assisted ventilation following delivery (Abdo et al., 2019).	↓
Neonatal intensive care unit admission	$N = 534,798$ ($n = 1$) (Abdo et al., 2019)	The study observed an inverse association between exposure to wildfire smoke during pregnancy and neonatal intensive care unit admission (Abdo et al., 2019).	↓
Birthweight	$N = 3,279,637$ ($n = 13$) (Fernández et al., 2023; Jung et al., 2023; Li et al., 2023; Zhang et al., 2023; Jones and McDermott, 2022; Li et al., 2022; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; Holstius et al., 2012; Prass et al., 2012)	Eleven of thirteen studies observed an adverse association between exposure to wildfire smoke during pregnancy and birthweight (Zhang et al., 2023; Jones and McDermott, 2022; Li et al., 2022; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; O'Donnell and Behie, 2015; Holstius et al., 2012; Prass et al., 2012).	↑
Gestational length	$N = 1,024,093$ ($n = 3$) (Jones and McDermott, 2022; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013)	Two of the three studies observed an adverse association between exposure to wildfire smoke during pregnancy and gestational length (Jones and McDermott, 2022; O'Donnell and Behie, 2013).	↑
High birthweight	$N = 60,054$ ($n = 1$) (Brew et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and high birthweight (Brew et al., 2022).	↑
Large-for-gestational age	$N = 7923$ ($n = 1$) (Fernández et al., 2023)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and large-for-gestational age birth (Fernández et al., 2023).	↑
Low birthweight	$N = 3,982,589$ ($n = 10$) (Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Requia et al., 2022a; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; Abdo et al., 2019; da Silva et al., 2014; O'Donnell and Behie, 2013)	Nine of the ten studies observed an adverse association between exposure to wildfire smoke during pregnancy and low birthweight (Zhang et al., 2023; Brew et al., 2022; Jones and McDermott, 2022; Requia et al., 2022a; Li et al., 2021b; McCoy and Zhao, 2021; Mueller et al., 2021; da Silva et al., 2014).	↑
Very low birthweight	$N = 227,948$ ($n = 1$) (Li et al., 2021b)	The study observed an association between exposure to wildfire smoke during pregnancy and very low birthweight (Li et al., 2021b).	↑
Preterm birth	$N = 4,870,316$ ($n = 6$) (Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Requia et al., 2022c; Abdo et al., 2019)	Five of the six studies observed an adverse association between exposure to wildfire smoke during pregnancy and preterm birth (Zhang et al., 2023; Heft-Neal et al., 2022; Jones and McDermott, 2022; Requia et al., 2022c; Abdo et al., 2019).	↑
Late preterm birth	$N = 330,884$ ($n = 1$) (Zhang et al., 2023)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and late preterm birth (Zhang et al., 2023).	↑
Very preterm birth	$N = 3,394,556$ ($n = 2$) (Zhang et al., 2023; Heft-Neal et al., 2022)	The two studies observed an adverse association between exposure to wildfire smoke during pregnancy and very preterm birth (Zhang et al., 2023; Heft-Neal et al., 2022).	↑
Extremely preterm birth	$N = 3,063,672$ ($n = 1$) (Heft-Neal et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and extremely preterm birth (Heft-Neal et al., 2022).	↑
Infant mortality	$N = 2,237,307$ ($n = 1$) (Pullabhotla et al., 2023)	The study observed no association between exposure to wildfire smoke during pregnancy and infant mortality (Pullabhotla et al., 2023).	
Pregnancy loss	$N = 75,262$ ($n = 1$) (Xue et al., 2021)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and pregnancy loss. (Xue et al., 2021).	↑
Sex ratio	$N = 287,688$ ($n = 1$) (O'Donnell and Behie, 2013)	The study observed no association between exposure to wildfire smoke during pregnancy and sex ratio (O'Donnell and Behie, 2013).	↔
Small-for-gestational age	$N = 594,852$ ($n = 3$) (Brew et al., 2022; Abdo et al., 2019)	One of the two studies observed an adverse association between exposure to wildfire smoke during pregnancy and small-for-gestational age (Abdo et al., 2019).	↑
Stillbirth	$N = 95,644$ ($n = 2$) (Xue et al., 2023)	One of the two studies observed an adverse association between exposure to wildfire smoke during pregnancy and stillbirth (Xue et al., 2023).	↑
Chromosomal anomalies			
Any chromosomal anomaly	$N = 16,825,497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and chromosomal anomalies (Requia et al., 2022b).	↔
Congenital anomalies			
Any congenital anomaly	$N = 16,825,497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies (Requia et al., 2022b).	↔
Circulatory system	$N = 16,825,497$ ($n = 1$) (Requia et al., 2022b)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and congenital anomalies of the circulatory system (Requia et al., 2022b).	↑
Digestive system	$N = 16,825,497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies of the digestive system (Requia et al., 2022b).	↔
Eyes, ears, face, and neck	$N = 16,825,497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies of the eyes, ears, face, and neck (Requia et al., 2022b).	↔

(*continued on next page*)

Table 2 (*continued*)

Outcome	Number of participants (number of studies)	Effect and effect direction[a]	
Genital organs	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and congenital anomalies of the genital organs (Requia et al., 2022b).	↑
Musculoskeletal system	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies of the musculoskeletal system (Requia et al., 2022b).	↔
Nervous system	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies of the nervous system (Requia et al., 2022b).	↔
Respiratory system	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and congenital anomalies of the respiratory system (Requia et al., 2022b).	↑
Urinary system	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and congenital anomalies of the urinary system (Requia et al., 2022b).	↔
Other congenital anomalies	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and other congenital anomalies (Requia et al., 2022b).	↑
Benign neoplasms/tumors	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed no association between exposure to wildfire smoke during pregnancy and benign neoplasms/tumors (Requia et al., 2022b).	↔
Cleft lip and cleft palate	$N = 16{,}825{,}497$ ($n = 1$) (Requia et al., 2022b)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and cleft lip and cleft palate (Requia et al., 2022b).	↑
Fetal gastroschisis	$N = 2{,}093{,}185$ ($n = 1$) (Park et al., 2022)	The study observed an association adverse between exposure to wildfire smoke during pregnancy and fetal gastroschisis (Park et al., 2022).	↑
Spina bifida	$N = 1{,}904{,}344$ ($n = 1$) (Park et al., 2021)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and spina bifida (Park et al., 2021).	↑
Obstetric health outcomes			
Gestational diabetes mellitus	$N = 594{,}852$ ($n = 2$) (Brew et al., 2022; Abdo et al., 2019)	One of the two studies observed an adverse association between exposure to wildfire smoke during pregnancy and gestational diabetes mellitus (Abdo et al., 2019).	↑
Gestational hypertension	$N = 594{,}852$ ($n = 2$) (Brew et al., 2022; Abdo et al., 2019)	One of the two studies observed an adverse association between exposure to wildfire smoke during pregnancy and gestational hypertension (Abdo et al., 2019).	↑
Induction of labor	$N = 60{,}054$ ($n = 1$) (Brew et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and induction of labor (Brew et al., 2022).	↑
Planned cesarean section	$N = 60{,}054$ ($n = 1$) (Brew et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and planned cesarean section (Brew et al., 2022).	↑
Unplanned cesarean section	$N = 60{,}054$ ($n = 1$) (Brew et al., 2022)	The study observed no association between exposure to wildfire smoke during pregnancy and unplanned cesarean section (Brew et al., 2022).	↔
Premature rupture of membranes	$N = 60{,}054$ ($n = 1$) (Brew et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and premature rupture of membranes (Brew et al., 2022).	↑
Early childhood health outcomes			
Prescription claim of lower respiratory infection medication	$N = 113{,}154$ ($n = 1$) (Dhingra et al., 2023)	The study observed an inverse association between exposure to wildfire smoke during pregnancy and prescription claim of lower respiratory infection medication (Dhingra et al., 2023).	↓
Prescription claim of systemic anti-inflammatory medication	$N = 113{,}154$ ($n = 1$) (Dhingra et al., 2023)	The study observed an inverse association between exposure to wildfire smoke during pregnancy and prescription claim of systemic anti-inflammatory medication (Dhingra et al., 2023).	↓
Prescription claim of upper respiratory infection medication	$N = 113{,}154$ ($n = 1$) (Dhingra et al., 2023)	The study observed no association between exposure to wildfire smoke during pregnancy and prescription claim of upper respiratory infection medication (Dhingra et al., 2023).	↔
Under-3 early (fetal, infant, and child) mortality	$N \approx 1{,}300{,}000$ ($n = 1$) (Jayachandran, 2009)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and under-3 early mortality (Jayachandran, 2009).	↑
Under-5 child mortality	$N = 228{,}661$ ($n = 1$) (Li et al., 2022)	The study observed an adverse association between exposure to wildfire smoke during pregnancy and under-5 child mortality (Li et al., 2022).	↑

[a] Effect direction: ↑ suggestive increased odds/risk of adverse outcome, ↓ suggestive decreased odds/risk of adverse outcome, ↔ inconsistent results or no statistically significant association.

municipality/day, there was an increase in the odds of low birthweight among infants of mothers residing in the Midwest (aOR, 1.001; 95% CI, 1.0001 to 1.002) and South (aOR, 1.02; 95% CI, 1.01 to 1.02) regions of Brazil. In the Midwest, an association was observed following exposure in the earlier trimesters. In the South, an association was observed for each trimester but was more pronounced for the later trimesters. In contrast, inverse associations were observed following exposure to wildfire smoke during trimesters 1 and 3 among infants of mothers residing in the Northeast (aOR, 0.996 to 0.997) and North (aOR, 0.9993) regions of Brazil (both statistically significant).

3.6.1.3. Meta-analysis and publication bias assessment of studies examining birthweight and low birthweight. Meta-analysis and publication bias assessment were only performed for outcomes examined by ≥3 studies that were methodologically similar and examined the same window of exposure. For this review, meta-analysis and publication bias assessment was performed for birthweight and low birthweight as outcomes by window of exposure (entire pregnancy, trimester 1, trimester 2, or trimester 3). The Egger's test showed no statistical significance (all P > 0.05) regardless of the outcome or window of exposure suggesting no evidence of publication bias (S4 Table).

The combined sample size for birthweight and low birthweight were 1,231,723 and 1,177,561 infants, respectively. A 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure was associated with a 16.18 g, 31.29 g, 21.40 g, and 5.08 g decrease in birthweight following exposure during the entire pregnancy, trimester 1, trimester 2, and trimester 3, respectively. In regard to low birthweight, a 21%, 29%, 55%, and 7% increased risk of low birthweight was associated with every 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during the entire pregnancy, trimester 1, trimester 2, and trimester 3, respectively. The overall meta-analysis found no statistically significant association between birthweight, low birthweight, and wildfire smoke-related $PM_{2.5}$ exposure during pregnancy, irrespective of the window of exposure. We observed high heterogeneity between the studies examining birthweight ($I_2 \geq 89.7\%$) and low birthweight ($I_2 \geq 97.2\%$) (S1 Figure and S2 Figure).

3.6.2. Preterm birth

Six studies investigated the association between wildfire smoke exposure during pregnancy and preterm birth (S2 Table) (Zhang et al., 2023; Brew et al., 2022; Heft-Neal et al., 2022; Jones and McDermott, 2022; Requia et al., 2022c; Abdo et al., 2019; Breton et al., 2011). Among these studies, six reported higher risk of preterm birth associated with higher exposure to wildfire smoke during pregnancy. Two studies reported a 31–48% increase in the risk (Zhang et al., 2023) and odds (Abdo et al., 2019) of preterm birth per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure (both statistically significant). Both studies also observed more pronounced positive associations following exposure to wildfire smoke during trimester 2 (aHR, 2.72; 95% CI, 2.48 to 2.98 and aOR, 1.86; 95% CI, 1.52 to 2.27, respectively) per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure (Zhang et al., 2023; Abdo et al., 2019). The former study by Zhang et al. (2023) in New South Wales, Australia, also included several stratified analyses. They reported significant associations by sex (male infants: aHR, 1.64; 95% CI, 1.51 to 1.78; female infants: aHR, 1.31; 95% CI, 1.19 to 1.44) and remoteness (major cities: aHR, 1.19; 95% CI, 1.10 to 1.29; inner region: aHR, 1.46; 95% CI, 1.30 to 1.65; outer region: aHR, 1.36; 95% CI, 1.10 to 1.70) as defined by the Australian Statistical Geography Standard Remoteness Structure (Australian Bureau of Statistics, 2021). Divergent seasonal effects were also observed. Infants of mothers who conceived during autumn and spring showed significant increases in the risk of preterm birth (aHR, 1.98; 95% CI, 1.83 to 2.14 and aHR, 144.48; 95% CI, 95.06 to 219.19, respectively) while infants of mothers who conceived during summer and winter demonstrated a lower risk of preterm birth (aHR, 0.24; 95% CI, 0.19 to 0.32 and aHR, 0.13; 95% CI, 0.08 to 0.23, respectively) per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure.

A study conducted in the United States by Heft-Neal et al. (2022) reported an increased risk of preterm birth per additional wildfire smoke day (0.5%; 95% CI, 0.41% to 0.59%), irrespective of trimester of exposure. When considering the intensity of wildfire smoke exposure, this effect was more pronounced among infants of mothers exposed to high (smoke days with $PM_{2.5}$ >10 μg/m^3) and medium (smoke days with $PM_{2.5}$ 5–10 μg/m^3) intensity wildfires (0.82% and 0.95%, respectively; statistically significant) (Heft-Neal et al., 2022). No statistically significant association was observed following exposure to low (smoke days with $PM_{2.5} < 5$ μg/m^3) intensity wildfire during pregnancy. Similar to Heft-Neal et al. (2022), Waldrop et al. (2023) also observed a comparable increase in the odds of preterm birth per additional wildfire smoke day (1.003%; $p < 0.0001$). Jones and McDermott (2022) reported a 1.2% increased risk of preterm birth among infants of mothers exposed to wildfire smoke during pregnancy compared to infants of unexposed mothers. This study also identified a more pronounced association following wildfire smoke exposure during trimester 2 (2.2%; $p < 0.05$) and following exposure to larger wildfires (>250,000 acres) during pregnancy (1.4%; $p < 0.01$) compared to infants of unexposed mothers.

Using a time-stratified case-crossover design, a Brazilian study compared the association of wildfire smoke exposure during pregnancy by region and trimester of exposure (Requia et al., 2022c). The highest increased odds of preterm birth were observed in the Southeast region (trimester 1: aOR, 1.41; 95% CI, 1.32 to 1.51; trimester 2: aOR, 1.27; 95% CI, 1.19 to 1.36; trimester 3: aOR, 1.39; 95% CI, 1.28 to 1.50) compared to the other trimesters of wildfire smoke exposure. When stratifying by sex, there was an increased odds of preterm birth; female infants of mothers exposed to wildfire smoke during pregnancy were consistently more likely to be born preterm compared to female infants of unexposed mothers. Similarly, a weaker association was found among infants of mothers in the South region (aOR, 1.05–1.06; statistically significant), but differences in the effect by sex were not observed. In the Midwest and North regions of Brazil, positive associations of preterm birth were only observed following exposure to wildfire smoke during trimesters 1 (aOR, 1.04; 95% CI, 1.01 to 1.07) and 2 (aOR, 1.06; 95% CI, 1.02 to 1.10), respectively. Few studies have explored the degree of preterm birth, such as late preterm birth, (Zhang et al., 2023) very preterm birth, (Zhang et al., 2023; Heft-Neal et al., 2022) and extremely preterm birth (Heft-Neal et al., 2022), following exposure to wildfire smoke during pregnancy. Per 5 μg/m^3 increase in $PM_{2.5}$ exposure, Zhang et al. (2023) reported an increased risk of late and very preterm birth by 46% and 77% (95% CI, 1.35 to 1.56 and 95% CI, 1.56 to 2.02, respectively). When stratifying by trimester of exposure, the risk of late and preterm birth was significantly more pronounced following trimester 2 exposure to wildfire smoke per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure (aHR, 1.81; 95% CI, 1.62 to 2.03 and 4.49; 95% CI, 4.05 to 4.97). Similarly, Heft-Neal et al. (2022) observed a 0.88% increased risk of very preterm birth per smoke day (95% CI, 0.52% to 1.24%) and significant elevation in the risk of very and extremely preterm birth following exposure to wildfire smoke during trimester 2 (1.45%; 95% CI, 0.96% to 1.95% and 1.51%; 95% CI, 0.60% to 1.08, respectively).

3.6.3. Gestational length

Three studies evaluated the association between wildfire smoke exposure during pregnancy and gestational length (Jones and McDermott, 2022; O'Donnell and Behie, 2015; O'Donnell and Behie, 2013) (S2 Table). Two of these studies observed an association between wildfire smoke exposure during pregnancy and gestational length. According to a study by Jones and McDermott (2022) exposure to wildfire smoke during pregnancy resulted in a decrease in gestational length by 0.59 days ($p < 0.05$) compared to infants of unexposed mothers. This negative association was primarily attributable to exposure during trimester 2 (−0.9 days; $p < 0.01$) and was more pronounced following exposure to

larger wildfires (range: −0.7 to −1.2 days; $p < 0.05$). Similarly, O'Donnell and Behie (2013) reported higher proportions of infants with shorter gestational lengths among the exposed group compared to the unexposed group, irrespective of trimester of exposure ($p < 0.05$).

3.6.4. Small-for-gestational age

Four studies investigated the association between wildfire smoke exposure during pregnancy and small-for-gestational age (Fernández et al., 2023; Brew et al., 2022; Abdo et al., 2019; Breton et al., 2011) (S2 Table). Abdo et al. (2019) reported a 22% higher odds of small-for-gestational age per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy (95% CI, 1.04 to 1.44), which was mainly observed for exposure during trimester 1 (aOR: 1.34; 95% CI, 1.01 to 1.79). No associations were observed among the other three studies (Fernández et al., 2023; Brew et al., 2022; Breton et al., 2011).

3.6.5. Stillbirth

Two studies evaluated the association between wildfire smoke exposure during pregnancy (Xue et al., 2023; Brew et al., 2022). A multi-country study by Xue et al. (2023) reported an 8% increase in the odds of stillbirths per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy (95% CI, 1.01 to 1.16). However, no association was observed for the other study (Brew et al., 2022).

3.6.6. Other perinatal outcomes

Some perinatal outcomes were only examined in individual studies (Fernández et al., 2023; Brew et al., 2022; Xue et al., 2021; Abdo et al., 2019) (S2 Table). One study by Abdo et al. (2019) reported a 49–93% lower odds of assisted ventilation following delivery per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy and when stratifying by trimester of exposure, this was observed for exposure to wildfire smoke during trimesters 1 and 2 (statistically significant). This study also found that per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure was associated with a 20–67% lower odds of neonatal intensive care admissions (statistically significant), particularly following exposure during trimester 2 (aOR, 0.68; 95% CI, 0.50 to 0.94) (Abdo et al., 2019).

A study by Brew et al. (2022) observed 16% higher odds of high birthweight following exposure to wildfire smoke during pregnancy in conjunction with the COVID-19 pandemic lockdown 2 and high birthweight (95% CI, 1.02 to 1.31) compared to infants of mothers unexposed to wildfire smoke during pregnancy and both COVID-19 pandemic lockdowns. One study by Fernández et al. (2023) observed a 69% higher risk of large-for-gestational age per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy. Another study investigated the association between wildfire smoke exposure during pregnancy and pregnancy loss. This multi-country study evaluated wildfire smoke exposure using three different methods and reported a 28% increased odds of pregnancy loss per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy (95% CI, 1.19 to 1.38) (Xue et al., 2021). No statistically significant associations were found for infant mortality (Pullabhotla et al., 2023) and sex ratio (O'Donnell and Behie, 2013).

3.7. Congenital and chromosomal anomalies

Three studies reported on wildfire smoke exposure and congenital anomalies (Park et al., 2021, 2022; Requia et al., 2022b) (S2 Table). Two studies by Park et al. (2021, 2022) examined wildfire smoke exposure in California, United States. One study observed a 27% and 23% higher risk of fetal gastroschisis among infants of mothers exposed to wildfire smoke during trimesters 1 and 2, respectively, compared to infants of unexposed mothers (statistically significant) (Park et al., 2022). This negative association was more pronounced among infants of mothers exposed to wildfire smoke during trimester 1 who resided 10–15 miles from a wildfire (aRR, 1.34; 95% CI, 1.02 to 1.75) compared to infants of unexposed mothers. The other study by Park et al. (2021) observed a greater risk of spina bifida among infants of mothers exposed to wildfire smoke during trimester 1 (aRR, 1.43; 95% CI, 1.11 to 1.84) compared to infants of unexposed mothers. These studies also included additional analyses to examine the association between pre-pregnancy exposure to wildfire smoke and found a 1.83- and 1.43-fold increase in the risk of fetal gastroschisis and spina bifida (95% CI, 1.13 to 2.95 and 95% CI, 1.11 to 1.84, respectively) compared to infants of unexposed mothers.

A study conducted in Brazil investigated the impact of wildfire smoke exposure during pregnancy on congenital anomalies of various organ systems, cleft lip and cleft palate, benign neoplasms and tumors, and chromosomal anomalies (Requia et al., 2022b). Per 10 wildfire records per municipality/day during trimester 1, there was an increased odds of congenital anomalies of the circulatory system among female infants in the Southeast region (aOR, 1.37; 95% CI, 1.03 to 1.82), genital organs among male infants in the South region (aOR, 1.08; 95% CI, 1.01 to 1.15), nervous system among infants in the Midwest region (any sex: aOR, 1.02; 95% CI, 1.01 to 1.03; female infants: aOR, 1.07; 95 CI, 1.04 to 1.11), and other congenital anomalies among male infants in the North region (aOR, 1.07; 95% CI, 1.02 to 1.12). Exposure to wildfire smoke during trimester 2 was associated with congenital anomalies of the respiratory system among infants in the North region (aOR, 1.14; 95% CI, 1.02 to 1.26), cleft lip and cleft palate among infants in the South region (any sex: aOR, 1.07; 95% CI, 1.001 to 1.14; male infants: aOR, 1.09; 95% CI, 1.003 to 1.18) and male infants in the Southeast region (aOR, 1.19; 95% CI, 1.02 to 1.37) per 10 wildfire records per municipality/day. This study found no statistically significant association between wildfire smoke exposure during pregnancy and other congenital (digestive system; eyes, ears, face, and neck; musculoskeletal system; urinary system) and chromosomal anomalies, benign neoplasms and tumors.

3.8. Obstetric outcomes

Brew et al. (2022) and Abdo et al. (2019) investigated the association between wildfire smoke exposure during pregnancy and obstetric outcomes, including gestational diabetes mellitus, (Brew et al., 2022; Abdo et al., 2019) gestational hypertension, (Brew et al., 2022; Abdo et al., 2019) mode of delivery (i.e., planned and unplanned cesarean section, and induction of labor), (Brew et al., 2022) and premature rupture of membranes (Brew et al., 2022) (S2 Table). Abdo et al. (2019) reported a 1.39- to 2.02-fold increase in the odds of gestational diabetes mellitus per 5 μg/m^3 increase in wildfire smoke-related $PM_{2.5}$ exposure during pregnancy and during trimester 1 (both statistically significant). In contrast, Brew et al. (2022) observed a 13% lower odds of gestational diabetes mellitus following exposure to wildfire smoke during pregnancy in conjunction with COVID-19 pandemic lockdown 2 (95% CI, 0.79 to 0.96) compared to infants of mothers unexposed to wildfire smoke and both COVID-19 pandemic lockdowns.

Induction of labor and unplanned cesarean section were associated with wildfire smoke exposure during pregnancy (aOR, 1.06; 95% CI, 1.01 to 1.11) and exposure to wildfire smoke during pregnancy in conjunction with the COVID-19 pandemic lockdown 2 (aOR, 1.15; 95% CI, 1.04 to 1.27) compared to infants of mothers unexposed to wildfire smoke and both COVID-19 pandemic lockdowns, respectively (Brew et al., 2022). Exposure to wildfire smoke during pregnancy was associated with a 14% increased odds of premature rupture of membranes (aOR, 1.14; 95% CI, 1.05 to 1.24) and exposure to wildfire smoke during pregnancy in conjunction with the COVID-19 pandemic lockdown 1 was associated with a 21% increased odds of premature rupture of membranes (aOR, 1.21; 95% CI, 1.07 to 1.37) compared to infants of mothers unexposed to wildfire smoke and both COVID-19 pandemic lockdowns (Brew et al., 2022).

3.9. Early childhood outcomes

One study by Dhingra et al. (2023) investigated the relationship between wildfire smoke during pregnancy and early childhood respiratory health. Respiratory prescription medication, serving as indicators of respiratory health, were examined as outcomes. This study reported a 3% lower risk of prescription claim of lower respiratory infection medication per additional wildfire smoke day for children of mothers exposed during trimester 1 (95% CI, 0.94 to 0.999). This study also observed a 4% and 5% lower risk of prescription claim of systemic anti-inflammatory medication for children of mothers exposed during trimester 1 (95% CI, 0.93 to 0.997) and trimester 2 (95% CI, 0.91 to 0.99), respectively. When stratifying by sex, there was an 8% and 6% lower risk of prescription claim of systemic anti-inflammatory medication for male children of mothers exposed during trimester 2 (95% CI, 0.87 to 0.98) and female children of mothers exposed during trimester 3 (95% CI, 0.88 to 0.99), respectively. No associations were observed for prescription claim of upper respiratory infection medication.

Child mortality was examined in two studies by Li et al. (2022) and Jayachandran (2009) (S2 Table). The study in Indonesia (Park et al., 2022) inferred under-3 early mortality from missing children in Census data. This study reported a significant decrease in cohort size of 1.1% or an estimated 14,300 child deaths associated with wildfire smoke exposure during pregnancy ($p < 0.05$) compared to children of mothers unexposed to wildfire smoke during pregnancy. The association was more pronounced following exposure during trimester 3 and among infants of mothers residing in poorer neighborhoods ($p < 0.01$) (Jayachandran, 2009). A multi-country study by Li et al. (2022) reported an increased under-5 child mortality risk of 15.98% (total effect) per 5 μg/m^3 increase in exposure to wildfire smoke-related $PM_{2.5}$ during pregnancy (95% CI, 2.33% to 32.36%). A mediation analysis found an indirect effect of 0.78% increase in risk of under-5 child mortality per 5 μg/m^3 increased exposure to wildfire smoke-related $PM_{2.5}$ during pregnancy (95% CI, 0.17% to 1.39%), of which 7.3% was mediated by change in birthweight.

4. Discussion

This systematic review examines the current literature on the impacts of wildfire smoke exposure during pregnancy on the health of pregnant women and their offspring. We analyzed 31 studies and identified overall significant associations between exposure to wildfire smoke during pregnancy and multiple adverse perinatal, obstetric, and early childhood health outcomes. Although results differed across studies, overall, there was a general consensus linking exposure to wildfire smoke during pregnancy with significant harm to both pregnant women and their offspring. There was consistent evidence indicating that wildfire smoke exposure during pregnancy was associated with an elevated risk of low birthweight and birthweight reduction, preterm birth, some congenital anomalies, some obstetric outcomes, and child mortality.

Our findings are consistent with several previous systematic reviews and meta-analyses, that examined a subset of the outcomes we considered, focusing on ambient PM exposure. A previous systematic review of eight studies examined the association between wildfire smoke exposure during pregnancy and adverse birth outcomes (e.g., low birth weight, preterm birth, gestational length, small-for-gestational age, under-3 early mortality, sex ratio) (Amjad et al., 2021). We performed a subsequent systematic review that not only provides an update but also expands on the previous review by exploring the potential impact of maternal wildfire smoke exposure on other perinatal outcomes as well as obstetric and early childhood health outcomes. In addition to the eight epidemiological studies included in the previous systematic review (Amjad et al., 2021), we identified an additional twenty-three studies, fifteen of which examined adverse birth outcomes. The authors of the previous systematic review reported that maternal wildfire smoke exposure was associated with adverse birth outcomes, including birthweight reduction and a higher risk of preterm birth. Our findings are consistent with a previously published systematic review on the association between wildfire smoke exposure during pregnancy and adverse birth outcomes. We also identified suggestive evidence of potential associations between maternal wildfire smoke exposure and other adverse health outcomes including small-for-gestational age, under-3 early mortality and under-5 child mortality.

Two individual meta-analyses by Yu et al. (2021) and Bai et al. (2020) respectively, found significant positive associations of cleft lip with or without cleft palate (pooled OR, 1.02; 95% CI, 1.005 to 1.03) per 5 μg/m^3 increase of ambient PM_{10} exposure during pregnancy (10 studies) (Yu et al., 2021), gestational hypertensive disorders per 5 μg/m^3 increase of ambient $PM_{2.5}$ exposure during pregnancy (pooled RR, 1.16; 95% CI, 1.02 to 1.34) (3 studies) (Bai et al., 2020), and gestational hypertension per 5 μg/m^3 increase of ambient PM_{10} exposure during trimester 1 (pooled RR, 1.05; 95% CI, 1.01 to 1.05) (4 studies) (Bai et al., 2020). Similar to the aforementioned studies, our findings revealed significant positive associations with some congenital anomalies, including fetal gastroschisis and spina bifida, following wildfire smoke exposure during pregnancy, and gestational diabetes mellitus and gestational hypertension following wildfire smoke-related $PM_{2.5}$ exposure during pregnancy.

Pregnant women are considered a high-risk group that is particularly vulnerable to harm as a consequence of exposure to wildfire smoke (Center for Disease Control and Prevention, 2021). Wildfire smoke-related air pollutants, including particulate matter, are hypothesized to have the potential to cross the blood-placental barrier, disrupt the circulation of blood between the mother and fetus, and directly impair the development of the growing fetus (Chen et al., 2021). Compared to ambient $PM_{2.5}$, the composition of wildfire smoke-related $PM_{2.5}$ has a higher fraction of ultrafine particulates (<0.1 μm in diameter), which have been shown to deposit deeper into the alveolar sacs of the lungs and have the ability to pass directly into the bloodstream (Schraufnagel, 2020). Increasing evidence indicates that maternal PM exposure leads to vascular inflammation, oxidative stress, cellular and endocrine dysfunction, which can result in a myriad of biological effects including placental stress and dysfunction, ultimately affecting fetal development during pregnancy (Basilio et al., 2022). Wildfire smoke comprises a greater mass composition of organic carbon and larger number of polar organic molecules and ultimately has a stronger oxidative potential compared to ambient air pollutants (Williams et al., 2013; Verma et al., 2009). Additionally, proinflammatory molecules, such as PAHs, are generated at higher concentrations in wildfire smoke-related $PM_{2.5}$ compared to ambient $PM_{2.5}$ due to higher combustion temperatures (Williams et al., 2013). Despite the proposed biologically plausible hypotheses explaining the potential association between wildfire smoke exposure during pregnancy and adverse health outcomes, the exact physiological pathways have yet to be confirmed.

To our knowledge, this is the first systematic review summarizing the association between wildfire smoke exposure during pregnancy and other adverse perinatal outcomes, beyond birthweight, preterm birth, and small-for-gestational age, as well as obstetric outcomes. We employed a comprehensive search strategy, reviewed by an experienced research librarian, to search multiple electronic databases and gray literature to identify relevant studies on wildfire smoke exposure during pregnancy and adverse perinatal, obstetric, and early childhood health outcomes. Furthermore, we also used backward and forward citation chaining to identify any potentially relevant studies not found by our comprehensive search strategy. We complied with the Cochrane and PRISMA guidelines for conducting and reporting systematic reviews. In accordance with the Cochrane guidelines, the screening, reviewing, data extraction, and risk of bias assessment of the identified studies were performed by two independent reviewers. We considered a wide array of health outcomes (e.g., congenital anomalies, gestational diabetes mellitus, gestational hypertension, mode of delivery, and under-5 child

mortality).

Despite these strengths, our overall findings were limited by the high methodological heterogeneity concerning study design, ascertainment method and definition of exposure, evaluated outcomes, and statistical approaches among the included studies, which precluded the pooling in the meta-analysis for some outcomes. Most studies used indirect markers or proxy measures of wildfire smoke exposure (i.e., spatial and/or temporal overlap with wildfire), which may not accurately reflect the true exposure for the mother nor the intensity and degree of exposure to wildfire smoke, and therefore disentangling the potential health impacts of wildfire smoke-related air pollutants from ambient air pollutants is challenging. While some studies attempted to directly estimate the concentration of wildfire smoke-related air pollutants (i.e., $PM_{2.5}$, PM_{10}, and CO), the relative contribution of wildfire smoke-related air pollutants, and its chemical components, from ambient air pollutants is difficult to determine accurately. This can result in over- or under-estimation of the observed associations between wildfire-specific air pollutant exposure and health outcomes, and likely can bias the magnitude of the associations. For one study in Thailand, we estimated the impact of wildfire smoke-related $PM_{2.5}$ from the observed association of PM_{10} and the outcomes. While we attempted to minimize uncertainty by using a time- and location-specific conversion ratio, we cannot rule out the possible over- or under-estimation of the reported associations. In addition to exposure to wildfire smoke during pregnancy, it is unclear whether increased temperature and/or maternal stress plays a role in the impacts of maternal wildfire smoke exposure on maternal and infant health, and disentangling the potential roles of these factors is another significant challenge. Some studies were unable to account for key sociodemographic confounders, including race/ethnicity, education, and/or socioeconomic status, which is a limitation leading to potential bias due to uncontrolled confounding. The sample size of some studies was small, particularly when considering adjustments and stratifications that were made, and therefore might have contributed to null associations in some cases. Furthermore, we cannot rule out the possible influence of bias due to temporary or permanent mobility patterns (i.e., evacuation, migration, residential mobility). None of the reviewed studies were able to account for mobility patterns and since most studies relied on maternal residence at the time of birth, potential exposure misclassification is highly probable.

5. Conclusion

Our systematic review summarized the current literature on the impacts of maternal exposure to wildfire smoke and adverse health outcomes in mothers and their offspring. The current evidence suggests that exposure to wildfire smoke during pregnancy is associated with significant risks concerning low birthweight and birthweight reduction, preterm birth, congenital anomalies, obstetric outcomes, and child mortality. Although there has been a significant increase in the number of well-designed studies evaluating the impacts of wildfire smoke exposure on human health in recent years, additional methodologically homogenous studies are needed to enable future meta-analyses to be performed. Although wildfires occur in many regions around the world, the degree of geographic representation in the current literature is severely limited. Therefore, additional studies conducted in other wildfire-prone regions are also warranted. Currently, there is a paucity of research on the potential differential health impacts by type of biomass burning (i.e., type of vegetation), the chemical constituents of emission, and fires at the wildland-urban interface, which can include burning of building materials (National Academies of Sciences et al., 2022). Future research is also needed to explore potential nonlinear responses, such as whether a given increment of wildfire smoke has the same relative impact on health risk across the range of potential exposure levels, as well as across various lag structures. It is also unclear what role other stressors, including social determinants of health, have on the impact of wildfire smoke exposure. Future studies should also consider using effect modification by other stressors to address this gap in knowledge. The public health impacts of wildfires on health will become more important as climate change continues to increase the frequency, duration, and intensity of wildfires.

Author contributions

Damien Foo conceptualized, designed, and coordinated the review, prepared the search strategy and performed the systematic search, screened and reviewed the search results, performed data extraction and risk of bias assessment, performed the meta-analysis, prepared the tables and figures, drafted the first draft manuscript, revised the manuscript, and approved the final manuscript. Seulkee Heo, Gursimran Dhamrait, Rory Stewart, Hayon Michelle Choi, and Yimeng Song screened and reviewed the search results, performed data extraction and risk of bias assessment, revised the manuscript, and approved the final manuscript. Michelle L. Bell conceptualized and designed the review, screened and reviewed the search results, revised the manuscript, and approved the final manuscript.

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Declaration of competing interest

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Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.117527.

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