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A narrative review of the effect of wildfire exposure on pregnancy & birth outcomes

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A NARRATIVE REVIEW OF THE EFFECT OF WILDFIRE EXPOSURE ON PREGNANCY & BIRTH OUTCOMES

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ABSTRACT

Wildfires pose a significant and growing threat to human health. Current trends in climate change predict that wildfire occurrence and severity will increase in the near future, and therefore the adverse health effects associated with wildfire and its air quality effects are becoming increasingly relevant. Even with current efforts to stem future rises in temperature, wildfire activity will continue to increase due to lags in the climate system itself. Thus, in addition to the known increase in mortality, respiratory, and cardiovascular risks, there is a growing need to investigate other health outcomes associated with wildfire smoke exposure, especially their effect on pregnancy and birth outcomes.

In order to provide a broad overview of the state of wildfire research on the topic of pregnancy and birth outcomes, this narrative review will summarize the existing literature on pregnancy and birth outcomes associated with wildfire smoke exposure, with consideration for the ambient air pollution literature that informs wildfire research. As research in this specific topic is still developing, a pattern of limitations to study designs is beginning to emerge, which will guide future research needs. Finally, practical considerations for implementing research findings into land management and public health policies that reduce wildfire exposure in order to mitigate the health risks associated with it will be explained.

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LIST OF ABBREVIATIONS

BU .... Boston University

BW .... Birth weight

CATT-BRAMS .... Coupled Aerosol and Trace Gas Transport Model to the Brazilian Developments of the Regional Atmospheric Modeling System

CEDS .... Community Emissions Data System

CMAQ .... Community Multiscale Air Quality Modeling System

EPA .... Environmental Protection Agency

GOES .... Geostationary Operational Environment Satellite System

INPE-CPTEC .... Center for Weather Forecasting and Climate Studies of the National Institute for Space Research

LBW .... Low birth weight

MERRA-2... Modern-Era Retrospective analysis for Research and Applications Version 2

MODIS .... Moderate Resolution Imaging Spectroradiometer

NOAA .... National Oceanic and Atmospheric Administration

$PM_{2.5}$ .... Particulate matter (2.5µm in diameter and smaller)

PM_{10} .... Particulate matter (10µm in diameter and smaller)

PTB .... Pre-term birth

SES .... Socio-economic status

SGA .... Small for gestational age

TOMS .... Earth Probe Total Ozone Mapping Spectrometer

USFS .... United States Forest Service

USGS .... United States Geological Survey

VLBW .... Very low birth weight

WUI .... Wildland-urban interface

INTRODUCTION

Wildfires in North America

Wildfires in North America have been increasing in frequency and intensity as a result of anthropogenic climate change. Places historically considered not prone to fire are burning, such as the temperate rainforests of the Olympic Peninsula in Washington in 2015, and records for the largest fires ever recorded by region are consistently being broken, such as the 2015 Carlton Complex Fire in Washington and the 2002 Biscuit Fire in Oregon that re-burned in the 2017 Chetco Bar Fire (Dennison et al., 2014; Halofsky et al., 2020). Increases in fire activity (measured via cumulative fire area, number of large fires, and fire-season length) can be attributed to a number of factors, but anthropogenic climate change accounts for over half of documented increases in fuel aridity since the 1970s. Consequently, the cumulative forest fire area burned has doubled since 1984 in the Western United States (Abatzoglou & Williams, 2016). As a result of increasing wildfire activity and declining urban air pollution, the fraction of summertime organic aerosols in the western US that are attributed to wildfires is increasing as well (Ridley et al., 2018).

Multiple studies suggest a link between climate, weather, wildfire, air quality, and human health. A warming climate with longer dry seasons contributes to the accumulation of increasingly arid fuels, which then contribute to larger and more frequent wildfires (Abatzoglou & Kolden, 2013; Dennison et al., 2014; Holden et al., 2018; Kitzberger et al., 2017; Littell et al., 2009; Reilly et al., 2017; Westerling, 2016; Westerling et al., 2003). This increased burning of biomass can then release harmful pollutants that may affect the health of nearby and downwind communities (Adetona et al., 2016; Dong et al., 2017; Hutchinson et al., 2018; Karanasiou et al., 2021; Künzli et al., 2006; Salimi et al., 2017; Tinling et al., 2016; Vicedo-Cabrera et al., 2016). While some degree of climate variability is natural and expected, it is widely believed that the current accelerated pace of climate change is due to anthropogenic sources (Berliner, 2022; Hansen & Stone, 2016; Trouet et al., 2006). Strong evidence suggests that this trend of longer and increasingly intense wildfire seasons will persist, and wildfire smoke will become more intense and widespread, thus continuing to increase adverse impacts on human health.

In addition to contributing to climate change, human activity in the wildland-urban interface (WUI) directly leads to increased intensity and length of wildfire seasons. The WUI consists of agricultural, industrial, and residential activities that encroach on nearby wildland ecosystems. The close proximity of humans and wildland forests increases the potential for harm to both people and forests. On the one hand, development along the WUI increases opportunities for people to ignite fires – as illustrated in Figure 1, which charts the contributions of various anthropogenic ignition sources in the Western US. WUI-related ignitions are the majority source of human-related ignitions in Mediterranean California and the Southern Semiarid Highlands; in the remaining ecoregions analyzed, industrial activity and infrastructure development associated with human activity (e.g. road, railroad, interstate, agriculture) are the majority contributor to anthropogenic wildfire ignition sources. Some studies have found that human-related ignitions start over 97% of wildfires that threaten homes and lead to tripling of the fire season length (Balch et al., 2017; Fusco et al., 2016; Mietkiewicz et al., 2020). On the other hand, the burning of forests is a natural process upon which many ecosystems depend in order to clear away underbrush and allow for new growth; however, wildfire management policies created in the early 1900s of aggressive fire suppression, coupled with warmer and drier summers, have led to the accumulation of dry underbrush on forest floors, creating a tinderbox for dangerously severe wildfires to erupt (Abatzoglou & Williams, 2016; Hessburg et al., 2015; Marlon et al., 2012). Human development in the WUI incentivizes fire exclusion practices that contribute to the buildup of fuels on the forest floor (Halofsky et al., 2020), leaving residents living in wildfire-prone areas of the WUI at constant risk of harm. This is a significant danger since, from 1992-2015, around 60 million homes were within or up to 1km away from a wildfire (Mietkiewicz et al., 2020).

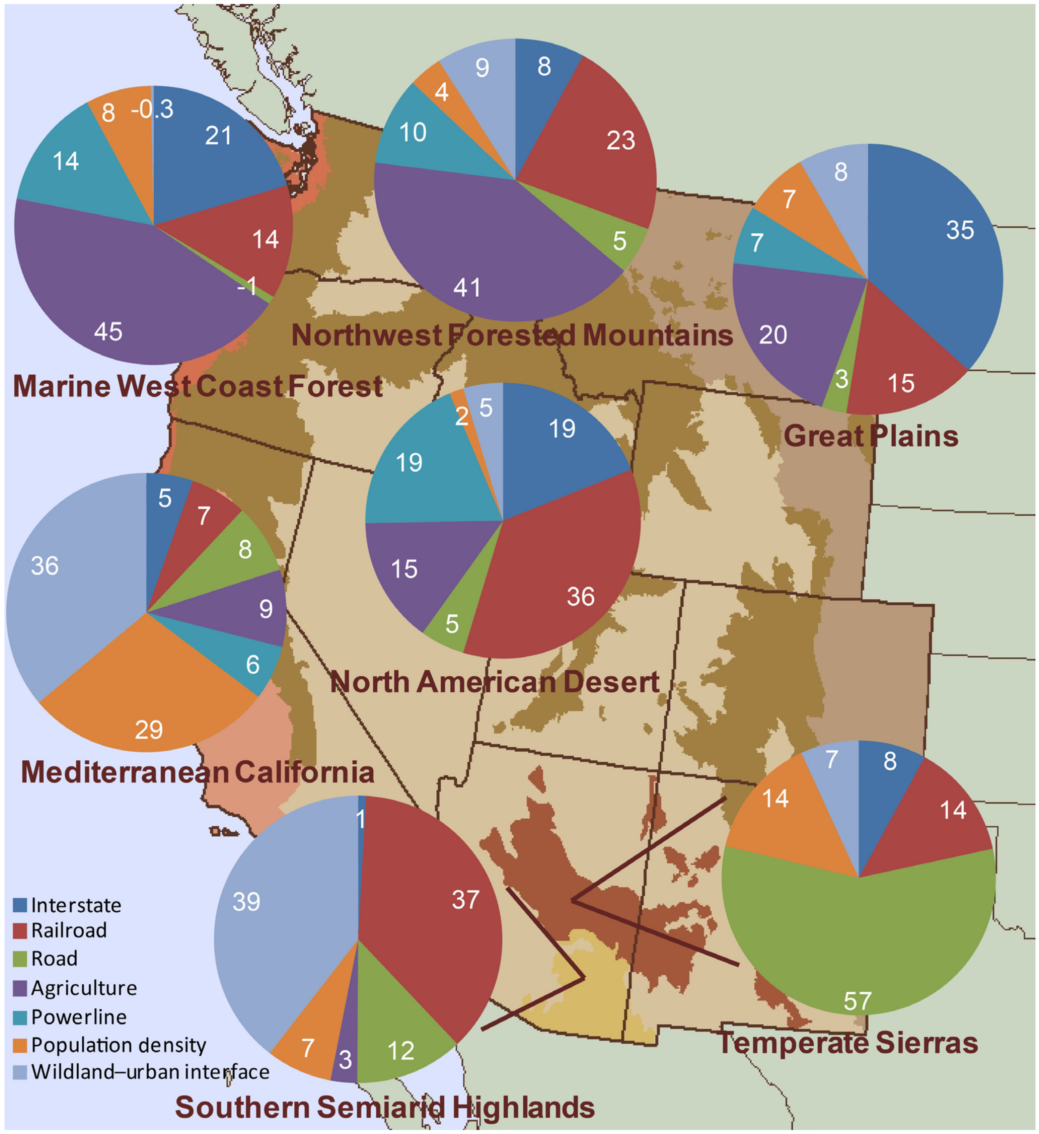

Figure 1 Top anthropogenic ignition sources for each ecoregion of the Western United States. Taken from (Fusco et al., 2016).

Impact of Wildfires on Human Health

One of the most important considerations when developing wildfire mitigation strategies is the threat they pose to human health and safety. The obvious dangers of wildfire include immediate damage to human health and property, health risks associated with exposure to wildfire smoke, and the mental health toll caused by experiencing a catastrophic event.

Wildfires place a significant economic burden on federal resources. One study estimated wildfires cost between $71.1B and $347.8B ($2016) annually in preparation, suppression, and direct and indirect economic effects (Thomas et al., 2017). Another study found that since federal spending on fire suppression has more than doubled in the last two decades, firefighting has consumed funds and resources at the expense of broader land management goals (Barbero et al., 2015).

Furthermore, beyond the direct costs of fire management, health costs associated with wildfire smoke exposure range between $11-20 billion/year in the continental US (Fann et al., 2018). Since the smoke plumes of wildfires have the potential to diffuse across large areas, they can affect large portions of the population across North America (Brey et al., 2018). Wildfire smoke is a significant and growing source of $PM_{2.5}$ in the atmosphere, particularly in the western US (O'Dell et al., 2019), and the air quality effects are associated with significant health risks. Indeed, exposure to wildfire smoke is becoming a problem for urban areas in other parts of the country as well. For example, during the 2020 wildfire season, smoke plumes from wildfires in western states were transported across the continent and were visible in New York and Washington DC (Andrew, 2020; Livingston, 2020).

Short-term exposure to wildfire smoke is strongly linked to all-cause mortality (Borchers Arriagada et al., 2020; Doubleday et al., 2020; Matz et al., 2020; Reid et al., 2016). There is evidence that exposure to wildfire smoke exacerbates many respiratory illnesses, including asthma, COPD, and respiratory infections (Alman et al., 2016; Borchers Arriagada et al., 2020; Fann et al., 2018; Liu et al., 2015; Liu, Wilson, Mickley, Dominici, et al., 2017; Matz et al., 2020; Stowell et al., 2019) and cardiovascular complications, though the evidence is less strong (Alman et al., 2016; Brook et al., 2010; Matz et al., 2020; Reid et al., 2016; Stowell et al., 2019). In addition to what is known, there is growing interest in studying the metabolic effects of short-term exposure to wildfire smoke, linking it to diabetic complications (Amjad et al., 2021; Yao et al., 2020), and an increasingly important topic in the health effects of wildfire smoke is the potential link between wildfire smoke exposure and pregnancy and birth outcomes, such as an increased risk in preterm birth and low birth weight (Amjad et al., 2021).

Finally, a less obvious health effect of wildfire smoke exposure is the toll it takes on mental health. Unsurprisingly, wildfire exposure has been linked to poor mental health (Verstraeten et al., 2021). A catastrophic event such as wildfire may lead to evacuation, lost loved ones, and lost property, causing a significant amount of stress on pregnant women, which can affect birth outcomes and the health of the child later in life (Dancause et al., 2011; Hobel et al., 2008). However, in comparison to studies on the cytotoxic effects of wildfire smoke, studies on the psychological effects of wildfire exposure are lacking. Furthermore, most studies focus on the psychological effects of these stressors rather than the potential direct impact of wildfire smoke on mental health.

Vulnerable Populations

Another critical consideration for developing wildfire policy is how the damaging effects of wildfire are unequally distributed across a population (Heft-Neal et al., 2022;

Jayachandran, 2009; Klepac et al., 2018; Liu, Wilson, Mickley, Dominici, et al., 2017; Prestemon et al., 2019). When considering the most effective strategies for mitigating damages from wildfires, it is important to target resources towards populations at the highest risk of adverse health outcomes due to wildfire exposure. These include people at higher risk of exposure, such as those who are required to work in wildfire conditions like wildland firefighters and agricultural workers, as well as people who are vulnerable due to physiological or socio-economic factors, such as those with pre-existing respiratory and cardiovascular disease (Amjad et al., 2021; Vicedo-Cabrera et al., 2016), those with low socio-economic status (Davies et al., 2018; Prestemon et al., 2019), children and the elderly (Holm et al., 2021; Liu, Wilson, Mickley, Ebisu, et al., 2017), and pregnant women (Amjad et al., 2021).

This narrative review will explore the adverse gestational and maternal health outcomes associated with wildfire exposure. Pregnant women have been identified as especially vulnerable to the adverse health effects of wildfire smoke, though the exact mechanism is unclear. Gestational outcomes associated with wildfire smoke exposure include increased rates of preterm birth and lower than average birth weight, and maternal outcomes include increased incidence of gestational diabetes and preeclampsia (Amjad et al., 2021; Drwal et al., 2019; Klepac et al., 2018). When considering the cumulative total of wildfire smoke exposure over the course of a lifetime (the exposome), prenatal exposure constitutes the earliest opportunity for exposure. Adverse birth outcomes due to prenatal wildfire smoke exposure can be the cause of health complications that accumulate through the rest of development, predicting disease outcomes later in life ("fetal origins hypothesis") (Almond & Currie, 2011; D. J. Barker, 1995; D. J. P. Barker & Osmond, 1986; Haikerwal et al., 2021; Howson et al., 2013; Hviid & Melbye, 2007; Mathewson et al., 2017; Osmond & Barker, 2000; Samaras et al., 2003). Though the evidence for many of the pregnancy and birth outcomes discussed is weak, a couple of outcomes are consistently strongly associated with wildfire exposure. As the foundation for studying the health effects of wildfires, the existing literature on health outcomes associated with exposure to ambient air pollution will also be considered. Many studies attempt to propose possible mechanisms of action, and the most commonly considered ones will be discussed. Next, common limitations of the existing studies will be identified and discussed. Finally, a few of the prevalent intervention strategies aimed at mitigating the adverse effects of wildfire exposure will be explained and evaluated.

PREGNANCY & BIRTH OUTCOMES

The most extensively studied birth metrics associated with wildfire exposure are birth weight and gestational duration. In the literature, birth weight is typically measured using "low birth weight" (LBW), though some studies use "small for gestational age" (SGA). Gestational duration is typically measured using "preterm birth" (PTB). Although specific criteria for each outcome varied across studies, there is generally a strong association found between wildfire exposure and low birth weight and a weaker but still statistically significant association found between wildfire exposure and preterm birth. Most studies attempted to identify a critical exposure window, during which the effects of wildfire exposure were more significant. The most commonly used exposure windows were the trimesters of pregnancy. However, exposures occurring immediately before pregnancy were also often considered. Since the trimester of pregnancy captures different critical stages of development, there is a reasonable scientific justification for these windows. However, the main limitation of this approach is that exposure windows that do not fall along the same cutoffs are excluded from consideration.

Much of the foundation for studying pregnancy and birth outcomes associated with wildfire comes from the literature on ambient air pollution exposure. For example, the choice of which birth outcomes to research is informed by the birth outcomes most strongly affected by exposure to ambient air pollution – PTB and LBW. Generally, the findings from wildfire studies are consistent with ambient air pollution research. A slight difference is that ambient air pollution suggests a slightly stronger association between air pollutants and LBW, whereas wildfire studies suggest a stronger association between wildfire smoke and PTB. This subtle difference may be due to slight differences in the way ambient air pollution and wildfire studies are conducted – ambient air pollution is often considered long-term/chronic and low-intensity exposure, whereas wildfire exposure is usually characterized as acute and short-term. There may also be differences in the composition of wildfire smoke compared to urban air pollution. Smoke composition is influenced by the type of fire and fuel, the age of the smoke plume, and various environmental factors such as humidity, wind, temperature, etc. These influence the chemical reactions that take place in the smoke plume, and the smoke composition as primary components such as carbon monoxide, nitrogenous compounds, sulfates, polycyclic aromatic hydrocarbons (PAHs), and volatile organic compounds (VOCs) are converted into secondary components such as ozone and PM (Kang et al., 2014; Strand et al., 2011). These differences in composition can then affect the toxicity and windows of susceptibility to the overall smoke plume.

Birth Weight

Birth weight-associated outcomes are generally measured using low birth weight (LBW), usually defined as weighing less than 2500g, though some studies also considered very low birth weight (VLBW) and small for gestational age (SGA), usually defined as <10th percentile value for gestational age and sex. Although LBW was more commonly used, it has been noted that SGA is a more sensitive metric since it accounts for fetal growth restriction and low birth weight due to delivery prior to gestational maturity (Bosetti et al., 2010). The findings of wildfire studies regarding low birth weight are summarized in Table 1. There was a general consensus among studies that wildfire smoke exposure during pregnancy is associated with LBW and SGA (Abdo et al., 2019; Breton et al., 2011; Cândido da Silva et al., 2014; Holstius et al., 2012; Jones & Berrens, 2021; Jones & McDermott, 2021; J. Li et al., 2021). However, one 2015 study on the Canberra bushfires in Australia found an association between maternal wildfire exposure and macrosomia (O'Donnell & Behie, 2015), which seems to support an opposing association of increased birth weight following gestational exposure to wildfire smoke. The study proposed that the observed increase in birth weight is caused by elevated maternal blood glucose levels due to stress (O'Donnell & Behie, 2015). It is important to note that macrosomia and LBW both pose health risks to the mother and child (Henriksen, 2008).

Findings were inconsistent regarding critical windows of exposure: a 2019 study of wildfire exposures in Colorado found that exposure in the first trimester was most significant (Abdo et al., 2019), while other studies found that exposure later in pregnancy, during the second and third trimesters were associated with greater reductions in birth weight (Breton et al., 2011; Cândido da Silva et al., 2014; Holstius et al., 2012; Jones & Berrens, 2021). A complicating factor is the observation that magnitude of fire size has a nonlinear relationship to the magnitude of the impact on birth weight (Jones & McDermott, 2021), possibly due to the increased magnitude of exposure.

These findings align with the literature on ambient air pollution and birth weight. LBW and SGA are consistently associated with ambient air pollution measured as outdoor air pollution exacerbation events, total suspended particles, $PM_{2.5}$, and PM_{10}

exposure (Bosetti et al., 2010; Klepac et al., 2018; X. Li et al., 2017; Melody et al., 2019a; Sun et al., 2016). Also consistent with findings from wildfire-specific studies, late-pregnancy exposure to ambient $PM_{2.5}$ (trimesters 2 & 3) is more often associated with low birth weight than other exposure windows considered (Melody et al., 2019a; Sun et al., 2016). The second trimester has been suggested as a critical period of fetal weight gain (Melo et al., 2008), which aligns with studies that found wildfire exposure during the second trimester particularly significant in increasing the risk of LBW.

Author(s)	**BW Metric**	**Exposure Window**	**Comments**
Abdo et al., 2019	LBW SGA	1st trimester	Weak association between 1st trimester exposure and SGA; estimated trimester data, exact birth date unavailable
Breton et al., 2011	-18g BW SGA	3rd trimester	No association for SGA
Candido da Silva et al., 2014	LBW	2nd & 3rd trimesters	Association with $PM_{2.5}$ and CO in a region of heavy deforestation, not specifically attributed wildfire; trimester data estimated based on date of birth
Holstius et al., 2012	BW	Any trimester: -6.1g 2nd trimester: -9.7g 3rd trimester: -7.0g	

Jones & Berrens, 2021	-18.2g BW	3rd trimester	Prescribed burns
Jones & McDermott, 2021	0.88pp LBW -16.56g BW	N/A	Nonlinear impact of megafire size on adverse birth outcomes
Li et al., 2021	LBW, VLBW	N/A (undefined gestational windows)	Sibling-matched case-control study in low- and middle-income countries
O'Donnell & Behie, 2015	+141g BW	N/A	Association between wildfire smoke exposure and increased birth weight

Table 1 Overview of wildfire studies focusing on birth weight outcomes.

Gestational Duration

Preterm birth (PTB) is usually defined as delivery at <37 weeks of gestation. However, some studies distinguished between severity of PTB (e.g., <22, 22-27, 28-32, and 32-37 weeks of gestation). The outcomes of wildfire studies focused on gestational duration are summarized in Table 2. There was a strong consensus among studies that maternal wildfire smoke exposure is significantly associated with PTB (Abdo et al., 2019; Heft-Neal et al., 2022; Jones & Berrens, 2021; Jones & McDermott, 2021; Requia et al., 2022). Exposures during the second trimester were most often reported as having the strongest association (Abdo et al., 2019; Heft-Neal et al., 2022; Requia et al., 2022), and exposure during the first trimester was also found to have a significant association with PTB (Requia et al., 2022).

This is consistent with the literature on ambient air pollution and PTB. Air pollution (measured via air quality exacerbation events, total suspended particles, elemental carbon, nitrous oxide, $PM_{2.5}$, and PM_{10}) is strongly associated with PTB (Bosetti et al., 2010; Fann et al., 2018; Klepac et al., 2018; X. Li et al., 2017; Melody et al., 2019a). Data regarding critical exposure windows are relatively heterogeneous, with the only consensus being a weak association between PTB and exposure at any point over the entire pregnancy (Fann et al., 2018; X. Li et al., 2017; Melody et al., 2019a).

Author(s)	PTB Metric	Exposure Window	Comments
Abdo et al., 2019	PTB	Entire pregnancy, 2^{nd} trimester	Associated with PTB occurrence; estimated trimester data, exact birth date unavailable
Breton et al., 2011	PTB	N/A	No association for PTB
Heft-Neal et al., 2022	Likelihood of PTB +0.88% (95% CI = 0.52-1.24%) <32 weeks +0.55% (95% CI = 0.05-1.15%) <28 weeks	2^{nd} trimester	Significantly mediated by baseline average smoke exposure
Jones & Berrens, 2021	-0.072 weeks of gestation	3^{rd} trimester	Prescribed burns
Jones & McDermott, 2021	+1.2pp PTB -0.08 weeks of gestation	N/A	Nonlinear impact of megafire size on adverse birth outcomes

Requia et al., 2022	Likelihood of PTB SE region: OR = 1.41 (95% CI = 1.31-1.51) N region: OR = 1.05 (95% CI = 1.01-1.09) mW region: OR = 1.04 (95% CI = 1.01-1.07) S region: OR = 1.05 (95% CI = 1.04-1.07) NE region: nonconvergent data	1st & 2nd trimester	

Table 2 Overview of wildfire studies focusing on gestational age/PTB outcomes

Less Studied Outcomes

Other less discussed health outcomes include fetal mortality/stillbirth and fetal malformation/birth defects, as well as maternal outcomes such as gestational hypertension, gestational diabetes, pregnancy loss, and placental disruption. Studies on these outcomes are scarce, so a few studies will be mentioned here. Table 3 presents a summary of the pregnancy and birth outcomes addressed in each study.

Fetal Mortality/Stillbirth

Fetal mortality/stillbirth was the third most mentioned birth outcome, though relative to PTB and LBW, data on fetal mortality are sparse. One study that examined the relationship between wildfire smoke exposure and early-life mortality (fetal, infant, and children under the age of 3) in Indonesia found that exposure in utero, especially in the one month before birth, was associated with increased early-life mortality (Jayachandran, 2009). They noted a subtle difference in effect by gender of the fetus, where males were more strongly affected when exposed in utero, possibly due to the hypothesis that male fetuses are more vulnerable, and females were more strongly affected when exposed immediately after birth, possibly due to gender discrimination. The study mentions that polycyclic aromatic hydrocarbons in wildfire smoke are a possible mediator for decreased survival, which is supported by studies on the effects of PAHs on the placenta (Drwal et al., 2019). A 2021 case-control study of the effects of the 2018 Camp Fire on non-human primates aligns with these findings, observing that early gestational exposure to wildfire smoke was associated with pregnancy loss (Willson et al., 2019). They found that during a particularly severe wildfire season, the ratio of live births to total conceptions that year was 82%, the lowest in 9 years, and that the group of exposed primates experienced double the rate of pregnancy loss to total conception compared to the group of non-exposed primates. Finally, the ambient air pollution literature on early-life mortality also agrees with these results, finding a weak association between air pollution exacerbation events during pregnancy and decreased fetal survival (Klepac et al., 2018; Melody et al., 2019a).

Fetal Malformation/Congenital Anomaly

Only one study was found that investigates the association between congenital anomalies and wildfire exposure. A 2021 population-based cohort study in California found that the risk of fetal gastroschisis more than doubled if the mother lived within 15 miles of a wildfire within 30 days before getting pregnant, and the risk increased by 28% if the mother was exposed in the first trimester of pregnancy (Park et al., 2022). This is consistent with the ambient air pollution literature on congenital anomalies: exposure to air pollution during pregnancy is associated with increased incidence of congenital anomalies, though the most common are cardiac anomalies and orofacial clefts as well as neural tube defects (Klepac et al., 2018; Vrijheid et al., 2011; Wang et al., 2019). However, it is noted that few other congenital anomalies are explored in the ambient air pollution literature relative to LBW and PTB, which may explain the lack of evidence for an association between the components of ambient air pollution and fetal gastroschisis.

Pregnancy Complications

Only one wildfire study was found in which pregnancy complications were considered. A significant positive association between exposure during the first trimester and over the entire pregnancy with gestational diabetes and gestational hypertension, with a 1ug/m3 increase in trimester average $PM_{2.5}$ exposure associated with a 14.4% increase in the incidence of gestational diabetes and a 14.8% increase in the incidence of gestational hypertension (Abdo et al., 2019). This is stronger than the information found on ambient air pollution, where associations between exposure to ambient air pollution and gestational hypertension/gestational diabetes are weak or inconsistent (Klepac et al., 2018; Melody et al., 2019a). As noted above, the differences may be due to different compositions of wildfire smoke components as compared to urban air pollution (Kang et al., 2014; Strand et al., 2011). Interestingly, a 2014 study in Taiwan showed that women who develop gestational diabetes are more susceptible to ozone exposure leading to preterm birth (Lin et al., 2015). This suggests an interaction between the different pregnancy and birth outcomes associated with wildfire exposure, adding another layer of complexity to the possible causal pathways.

Placental Disruption

Disruption of placental development was mentioned in one review, though briefly. Studies on polycyclic aromatic hydrocarbons, which are present in significant amounts in wildfire smoke, suggest that they can disrupt placental formation, angiogenesis, and hormone signaling, thereby affecting fetal development (Drwal et al., 2019). However, while there were no wildfire studies found that specifically studied placental disruptions, it is noted that a study on air pollution improvement events and various placental disruptions such as pre-labor rupture of membranes, placental abruption, placenta praevia, and placenta accreta found no association between the two (Melody et al., 2019a). At the interface between mother and fetus, it is likely that the placenta plays a critical part in mediating all effects of maternal wildfire exposure on the growing fetus. This is noted by most wildfire studies in their discussion of possible etiologic pathways through which maternal wildfire smoke exposure may lead to observed health outcomes (Amjad et al., 2021; Heft-Neal et al., 2022; Holstius et al., 2012; Jayachandran, 2009; Jones & Berrens, 2021; Park et al., 2022; Requia et al., 2022; Willson et al., 2019), as well as ambient air pollution studies discussing the same topic (Hyder et al., 2014; Klepac et al., 2018; Melody et al., 2019a; Rappazzo et al., 2015; Sapkota et al., 2012).

Author(s)	Outcome metric	Comments
(Abdo et al., 2019)	Pregnancy complications (gestational diabetes, gestational hypertension)	Associated with exposure in the 1st trimester; estimated trimester data, exact birth date unavailable
(Jayachandran, 2009)	Fetal mortality	Broad study of early-life mortality during the 1997 wildfires across Indonesia
(Willson et al., 2019)	Fetal mortality	2018 Camp Fire on non-human primates
(Park et al., 2022)	Congenital malformation (fetal gastroschisis)	Strongest association with exposure during the 30 days before becoming pregnant and during the 1st trimester

Table 3 Overview of wildfire studies that mention other pregnancy and birth outcomes.

PROPOSED MECHANISMS OF ACTION

Since observational studies examining associations between wildfire smoke exposure and adverse birth outcomes are observational by nature, almost every study mentioned a potential causal mechanism for the associations they found. The most frequently-proposed mechanisms are discussed in the following sections.

Maternal Oxidative Stress & Cytotoxicity

By far, the most commonly discussed mechanism through which maternal wildfire smoke exposure is thought to affect birth outcomes is via oxidative stress on the mother. Wildfire smoke is widely shown to have strong associations with poor respiratory and cardiovascular outcomes (Black et al., 2017; Navarro et al., 2018; Pope et al., 2006; Pope & Dockery, 2006; Williams et al., 2013), and there is growing evidence for an association with metabolic disruption (Johnston et al., 2019; Semmens et al., 2016b). As illustrated in Figure 2, wildfire combustion products are small enough to penetrate deep into the lung and reduce lung function and induce an irritant response (Adetona et al., 2016; Black et al., 2017; Guyon et al., 2005; Liu et al., 2015; Wegesser et al., 2010; Williams et al., 2013). Pregnant women are potentially more susceptible to respiratory effects of wildfire smoke exposure since they have increased tidal volume and oxygen consumption as an adaptation to pregnancy (Chang & Streitman, 2012; Kolarzyk et al., 2005). The systemic effects of respiratory irritation include inflammation in the airways, an increase in acute-phase proteins, and changes in blood pressure (Aghasafari et al., 2019).

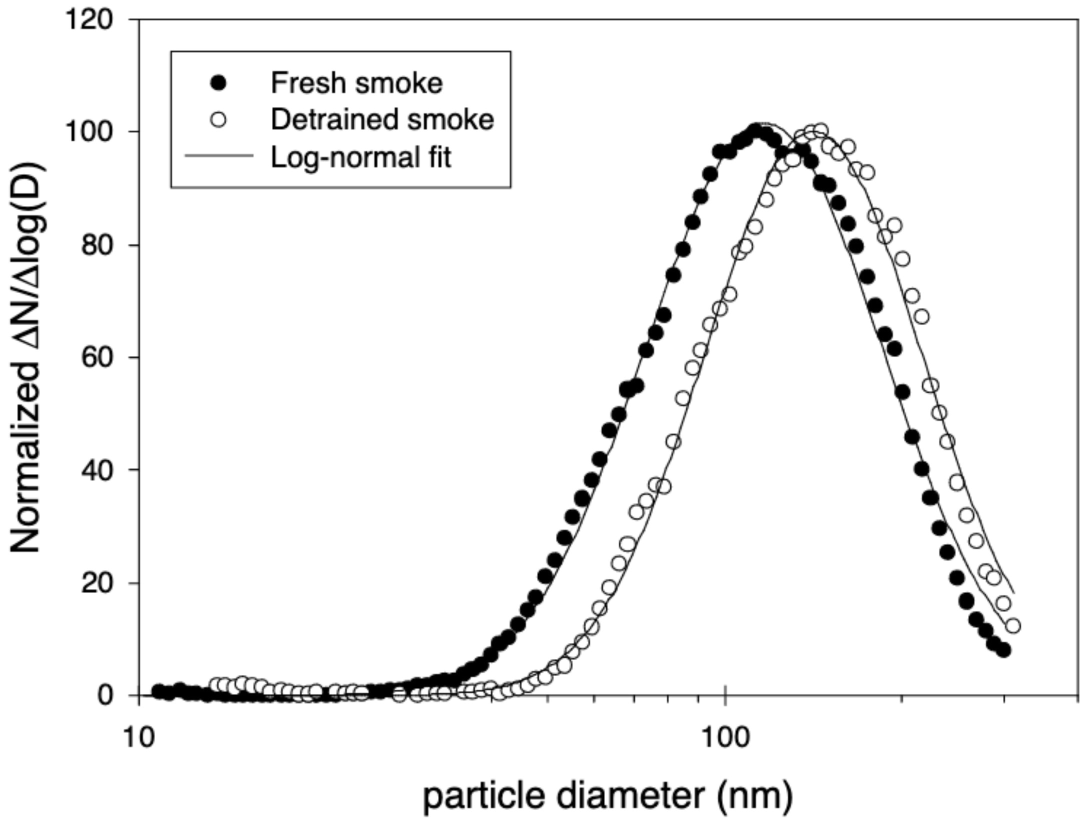

Figure 2 Aerosol particle size distribution of a fresh smoke plume (black dots) and an older detrained/emitted smoke plume that has undergone recomposition by chemical reactions with clouds (white dots). Particles 0.5µm and smaller are the ideal size for deep respiratory penetration. Taken from (Guyon et al., 2005).

Physiological changes in the mother are likely to affect the fetus, and the most often mentioned pathway is through the interference of oxidative stress on maternal-fetal circulation (Bosetti et al., 2010; Glinianaia et al., 2004; Holstius et al., 2012; Murphy et al., 2021). It is plausible that wildfire smoke exposure disrupts maternal-fetal circulation, resulting in reduced nutrient and oxygen exchange, which then affects fetal growth. Maternal-fetal circulation is also a route for endocrine exchange, which is another route through which systemic changes in the mother may affect fetal development. The

Australian study, which found an association between maternal wildfire smoke exposure and macrosomia, suggested that elevated levels of cortisol in maternal blood lead to increases in blood glucose and subsequently excessive growth of the newborn(O'Donnell & Behie, 2015). A study in China found a correlation between elevated C-reactive protein and complement C3 levels, markers for inflammation, in the mother and PTB (Huang et al., 2020).

Another possible route by which maternal systemic oxidative stress could affect birth outcomes is by increasing the risk of pregnancy complications. There is a strong association between pregnancy complications and adverse birth outcomes, such as the association between maternal hypertensive diseases and preterm birth, fetal growth restriction, and perinatal death (Pedersen et al., 2014). It is plausible that maternal complications associated with wildfire exposure may lead to the adverse birth outcomes observed. In 2019, the Hazelwood Health Study found that smoke exposure was not linked to LBW or PTB, but mothers who experienced gestational diabetes and gestational hypertension were found to deliver newborns with increased birth weight (Melody et al., 2019b). However, it is important to note that the association between wildfire smoke exposure and pregnancy complications is very weak when compared to its association with birth outcomes such as preterm birth and low birth weight, but also that pregnancy complications like gestational hypertension and preeclampsia are far less studied.

Stress & Epigenetic Modifications

The second most suggested hypothesis for how maternal wildfire smoke exposure leads to adverse birth outcomes is via psychological stress. There is evidence for psychological stressors being linked to adverse birth outcomes, especially birth weight and gestational length (Dancause et al., 2011; Lazinski et al., 2008). Most studies suggest an epigenetic mechanism. A study on bushfires in Australia studied a few methylation markers linked to various adverse health outcomes in the newborn, including PTB and identified FOXP3 methylation as associated with bushfire smoke exposure (Murphy et al., 2021). There is also some evidence for ambient air pollution affecting birth outcomes via epigenetic markers associated with stress (Liu et al., 2019), and some of these epigenetic markers were also associated with placental health (Non et al., 2012). It is possible that maternal stress could induce epigenetic modifications that subsequently alter the health of the placenta, which then influences fetal development.

Direct Cytotoxicity

A third theory is that chemical compounds from wildfire smoke directly affect fetal development through transplacental exposure (Amjad et al., 2021; Cândido da Silva et al., 2014; Glinianaia et al., 2004). Pregnant women may be especially vulnerable to the toxic effects of air pollution due to the high levels of cell-proliferation and organ development, as well as fluctuating fetal metabolic needs (Selevan et al., 2000). There are many studies characterizing the components of wildfire smoke (Aguilera et al., 2020; Kang et al., 2014; Strand et al., 2011), and from the ambient air pollution literature, many studies can be found detailing the toxicity profiles of each of those components (Drwal et al., 2019; Rohr & Wyzga, 2012). Studies have found that DNA adducts found in the maternal blood and placenta are associated with increased LBW and PTB (Perera et al., 1999). It is reasonable to propose that toxins from wildfire smoke may enter the maternal circulation and subsequently enter the fetal circulation. However, studies that consider this route of fetal exposure often lack discussion of the placenta and the filtering function it serves. Only one review was found that comprehensively discusses the effect of PAHs on the placenta (Drwal et al., 2019). The review notes that not only do PAHs have toxic effects on placental cells and disrupt placental formation, angiogenesis, development, and hormone signaling (Handwerger & Freemark, 2000; Le Vee et al., 2014; Z. Li et al., 2010; Mittal et al., 2007; Zhang et al., 2016) but PAHs have been found to cross the placental barrier (Autrup & Vestergaard, 1996; Sanyal et al., 1994)(Autrup and Vestergaard, 1996; Perera et al., 1999; Sanyal and Li, 2007) and therefore can directly disrupt fetal development.

Although this mechanism of gestational exposure leading to adverse birth outcomes is often mentioned, it remains relatively unexplored in comparison to the other mechanisms discussed previously. In order to further develop this potential route of fetal exposure, further research is needed on many aspects of the process: characterizing the chemical components of wildfire smoke and their evolution over time, uptake and bioavailability of smoke toxins in the maternal and fetal systems, and toxicity assessments of the constituents of wildfire smoke specifically.

COMMON LIMITATIONS ACROSS STUDIES

Most studies suffered from a few common methodological limitations. While some are unavoidable due to the nature of wildfires as unpredictable in location, timing, and severity, others can be mitigated through study design or improvements in measurement technology. Two of the most commonly mentioned limitations will be discussed below.

Exposure Assessment

By far, the most mentioned limitation in wildfire studies was the difficulty of exposure assessment. Measuring maternal wildfire smoke exposure is a complex, multi-step process. Generally, studies first characterize smoke levels in a region over a certain period of time, then use birth data to define a sample population, and finally define an "exposure" as smoke levels in the region of the mother's residence rising above a certain threshold. Each of these steps to define exposure can be achieved through a variety of methods, leading to heterogeneity across studies when it comes to exposure assessment. Table 4 summarizes the exposure assessment methods utilized by the wildfire studies cited and demonstrates this point. Inconsistency in exposure assessment is also an often-mentioned issue in studies on ambient air pollution. Of these steps, measuring wildfire smoke was noted to be especially complex, particularly due to the difficulty of disentangling the effects of wildfire smoke from ambient air pollution.

The most popular methods of measuring smoke levels were via direct measurement like at a ground station (Abdo et al., 2019; Holstius et al., 2012; Jones & Berrens, 2021; Requia et al., 2022; Willson et al., 2019) by satellite imaging (Abdo et al., 2019; Heft-Neal et al., 2022; Jayachandran, 2009; J. Li et al., 2021; Requia et al., 2022), using modeling software (Abdo et al., 2019; Cândido da Silva et al., 2014; J. Li et al., 2021; Liu, Wilson, Mickley, Dominici, et al., 2017; Requia et al., 2022), or simply as a function of distance from a wildfire (Jones & McDermott, 2021; Park et al., 2022) – many studies use some combination of these methods. Some studies used a more complex construction of smoke days, such as "smoke waves" (Liu et al., 2016; Liu, Wilson, Mickley, Ebisu, et al., 2017; Requia et al., 2022), to characterize smoke levels. Each of these methods has strengths and drawbacks. Ground station measurement is possibly the most accurate real-time measure of smoke levels; however, the concentration of measurement stations in urban areas results in difficulty disentangling the contribution of urban air pollution from that of wildfire smoke, as well as low resolution in rural regions where wildfires are of greatest concern. Satellite imaging can provide accurate information at a relatively high resolution for a large geographical region, but it cannot distinguish between ambient air pollution and wildfire smoke, cannot provide an accurate estimate of ground-level smoke, and becomes much less accurate when weather effects interfere with the smoke plume. Models are limited by the accuracy of the model, and verification is difficult if there are no ground measurements to compare against. Additionally, the lack of a standard model creates difficulty when comparing between studies. Finally, distance from wildfire provides a simple and functional metric, though it is generally a very rough estimate, as smoke levels are generally not a simple function of distance (Aguilera et al., 2020; Strand et al., 2011). One benefit of having many different methods of measuring smoke is the ability to capture many different characteristics of the smoke plume; however, the main limitation is that it makes the comparison between studies difficult.

Almost all of these methods of measuring wildfire smoke struggle to distinguish between wildfire smoke pollution and ambient air pollution. Generally, this was only achievable through models that collect data on the baseline level of air pollution and extrapolate to periods of wildfire smoke to estimate the contribution of ambient air pollution (Heft-Neal et al., 2022; Park et al., 2022; Wu et al., 2006). While this is an effective means of separating wildfire smoke from ambient air pollution, it is likely that further research into the differences between the composition of wildfire smoke and urban air pollution would provide ground stations with the capability of characterizing and attributing sources of air pollution. Real-time measurements could provide data points that would significantly improve the accuracy of modeled ambient air pollution levels. Interactions between the effects of wildfire smoke and ambient air pollution highlight the importance of considering them as separate variables. One study found that exposure to higher levels of baseline air pollution had a moderating effect on sensitivity to wildfire smoke, diminishing the adverse effects of acute wildfire smoke exposure (Heft-Neal et al., 2022). Older studies did not generally account for these effects (Abdo et al., 2019; Holstius et al., 2012; Liu, Wilson, Mickley, Ebisu, et al., 2017), while more recent studies took it into consideration more frequently (Heft-Neal et al., 2022; Murphy et al., 2021; Park et al., 2022). As wildfires become an increasingly larger proportion of air pollution sources, understanding the differences between the two can aid in predicting changes in the impact of air pollution on population health.

Adding another dimension to measuring wildfire smoke is the question of how smoke is identified. Most studies use $PM_{2.5}$ and PM_{10} levels as the proxy for measuring smoke, however chemical composition studies have shown smoke to be more complex. The composition of wildfire smoke depends on a multitude of factors, including fuel type, humidity, temperature, and other environmental and weather conditions (Naeher et al., 2007; Urbanski, 2013). The primary components of wildfire smoke include combustion products such as carbon monoxide, nitrogen oxides, polycyclic aromatic hydrocarbons, sulfates, and carbon components (Kang et al., 2014). Furthermore, wildfire smoke reacts with other components in the plume and atmospheric components, producing intermediate species that change the composition of the smoke plume over time. Currently, a particular chemical species of concern is ozone, which tends to spike in communities located downwind of wildfire (Black et al., 2017; Dreessen et al., 2016; Kang et al., 2014; Wigder et al., 2013), and has been associated with a multitude of adverse health effects (Koman & Mancuso, 2017; Ostro, 1993; Zhao et al., 2018a). Thus, using $PM_{2.5}$ or any single indicator to measure wildfire smoke cannot fully and accurately capture a smoke plume and its health ramifications as it disperses over time and space. Smoke composition studies are critical to developing the ability to measure wildfire smoke and also provide an opportunity to capitalize on existing ambient air pollution research. Since many of the components of wildfire smoke are also present in ambient air pollution, where detailed toxicity information has already been researched (Drwal et al., 2019; Koman & Mancuso, 2017; Ostro, 1993; Rohr & Wyzga, 2012; Zhao et al., 2018b), projections of health risks caused by wildfire smoke can be estimated by simply connecting individual components of wildfire smoke to their toxicity profiles and weighting by the proportion of the smoke plume it accounts for.

Another source of error in studies comes from pregnancy data. Almost all studies drew pregnancy, birth, and demographic data from databases of birth records, occasionally supplemented by surveys distributed to the mothers. This method of retrieving birth information is vulnerable to the typical issues of inaccurate or incomplete records. For instance, most studies note that while the mother's residential zip code was used to determine whether she was exposed to wildfire smoke based on smoke levels in the region, there is the possibility that her residential zip code did not correspond to her true location throughout pregnancy (Amjad et al., 2021; Heft-Neal et al., 2022; J. Li et al., 2021; Park et al., 2022; Requia et al., 2022). Thus, it is possible that personal exposure assessments are inaccurate. Other methods for measuring exposure have been proposed, such as by detection of biomarkers in blood and urine (Z. Li et al., 2010), but suffer the same drawbacks as the current method and are difficult to implement on a large scale. Given the infeasibility of obtaining a large quantity of accurate exposure data at such high resolution, there does not seem to be much room for improvement. One study even noted exposure misclassification as a potential strength in their analysis, as inaccurate zip codes biased their analysis towards the null (Park et al., 2022). Importantly, most studies included a very large sample population, diluting the effect of potential inaccuracies in individual exposure assessments.

Confounding Factors and Other Analytical Challenges

Another obstacle that was mentioned in almost every study is accounting for complicating factors. Most studies accounted for commonly considered and easily measurable variables, such as maternal demographic information and seasonality, but more complex variables, such as baseline maternal air pollution exposure and interactions between measured outcomes, were inconsistently incorporated across studies – this is likely due to differences in consideration and the complexity of identifying and measuring these variables. A list of the variables considered in each study is presented in Table 4.

Confounding variables that were simple to measure include maternal demographic information (age, race, BMI, geographic location, alcohol consumption, smoking status, and education/income as an indicator of socioeconomic status/SES) and seasonality/timing of pregnancy. When considered independent to wildfire smoke exposure, each of these variables is associatedwith the measured outcomes of decreased birth weight and gestational duration to varying degrees (MacLeod & Kiely, 1988). Several studies demonstrated that these variables can also affect vulnerability to wildfire smoke: population-based studies have found an association between low SES and increased likelihood of wildfire smoke exposure (Jones & Berrens, 2021; J. Li et al., 2021; Liu, Wilson, Mickley, Ebisu, et al., 2017; Prestemon et al., 2019), and one study on outdoor-housed female rhesus monkeys found that low social status correlated with worse respiratory outcomes associated with wildfire smoke exposure (Bai et al., 2021).

Most of these simple variables were accounted for in statistical analyses (Holstius et al., 2012; Requia et al., 2022; Willson et al., 2019).

Maternal variables with potentially more complex interactions with wildfire exposure and the measured birth outcomes were often noted but not consistently incorporated into statistical analyses, likely because their interactions with wildfire exposure are not fully understood. For example, maternal smoking status has a well-established association with pregnancy and birth outcomes (Delpisheh et al., 2006), but it is only accounted for in 7 out of 13 wildfire studies. Upon investigating the interaction between smoking status and wildfire exposure, an article on the 2019-2020 bushfires in Australia associated maternal smoking status found increased sensitivity to bushfire exposure on adverse pregnancy and fetal outcomes (Kumar et al., 2021). They proposed that this was due to an increased dose of pollutants found in tobacco and wildfire smoke. In contrast, baseline maternal air pollution exposure likely interacts with the measured exposure and outcomes through a similar mechanism, but was found to have a moderating effect on the association between wildfire smoke exposure and adverse pregnancy and birth outcomes (Heft-Neal et al., 2022, p.).

Interactions between the different birth outcomes being studied is another complicating factor. For example, the primary outcomes of interest, preterm birth, and low birth weight, are not fully independent as babies born before gestational term may not have achieved a stable weight yet, making them more likely to be under-weight (Salomon et al., 2007); therefore, one study noted the metric small for gestational age (SGA) as a more accurate indicator of fetal growth restriction, since it accounts for the duration of gestation (Bosetti et al., 2010). As the placenta plays such a critical role in interfacing between the fetus and the mother throughout development, placental disruption is associated with a variety of adverse growth and birth outcomes (Drwal et al., 2019; Nordenvall & Sandstedt, 1990). Other outcomes such as fetal gastroschisis are associated with an increased risk of growth restriction, PTB, and stillbirth (Bergholz et al., 2014; Bradnock et al., 2011; Burge & Ade-Ajayi, 1997; O'Connell et al., 2016). Curiously, the Hazelwood Health Study on the 2014 fire in Victoria, Australia, found no association between smoke exposure and PTB/LBW, but that mothers who developed gestational diabetes were more likely to deliver newborns with higher birth weight (Melody et al., 2019b). This is consistent with another Australian study that found an association between wildfire exposure and macrosomia (O'Donnell & Behie, 2015), suggesting maternal glucose dysregulation as the potential mechanism for increased birth weight. In some cases, the nature of birth outcomes themselves introduced biases into the data. It was noted that in studies that attempted to identify gestational windows of exposure especially sensitive to increasing the risk of PTB, preterm delivery sometimes resulted in a lack of data on late-pregnancy exposures and created a bias against late-pregnancy exposure in association with preterm birth (Heft-Neal et al., 2022). A few studies also noted that since fetal mortality is a potential outcome of exposure, exclusion of non-live births introduces a survivor bias into the data analysis (Jayachandran, 2009; J. Li et al., 2021; Melody et al., 2019a; Willson et al., 2019). Clearly, the causal relationships between wildfire smoke exposure and various pregnancy and birth outcomes are complex, and further research is required to elucidate their relationships.

Author(s)	**Exposure measurement method**	**Variables analyzed**
(Abdo et al., 2019)	NOAA satellite imagery-based Hazard mapping system + spatial interpolation of ground-based $PM_{2.5}$ monitor data from US EPA Air Quality System matched to maternal zip code	Maternal SES (measured via income/education) & smoking; normalized temperature; seasonality by calendar month of birth; gestational age for LBW & secondary outcomes
(Breton et al., 2011)	Data from monitoring network + MODIS satellite light extinction, meteorological, & smoke data assigned by location	Data unavailable
(Cândido da Silva et al., 2014)	Daily averages derived from CATT-BRAMS model at INPE-CPTEC, assigned based on maternal primary residence	Seasonality/month of birth, gestational age (for LBW outcome), maternal SES (measured via education)
(Heft-Neal et al., 2022, p.)	NOAA Hazard Mapping System Fire and Smoke Product based on satellite images from GOES + machine learning model	Baseline ambient air pollution exposure, maternal SES (measured via income/education & location of birth)

	estimates of surface $PM_{2.5}$ concentrations across 1x1km grid, assigned at zip-code level	
(Holstius et al., 2012)	MODIS satellite imagery + PM monitoring reports from CA Department of Forestry & Fire Protection, assigned based on temporal overlap between wildfire exposure window & gestational intervals	Gestational duration, seasonality, maternal SES (measured by education)
(Jayachandran, 2009)	TOMS satellite monitoring data interpolated based on 100km radius of subdistricts, exposure assigned by location	Maternal SES (measured via food consumption per capita, healthcare providers per capita), type of cooking fuel, rural/urban locality
(Jones & Berrens, 2021)	4km grid cell ground-level $PM_{2.5}$ measurements, derived from US EPA CMAQ model with data on fire emissions and prescribed burn area estimates from	Maternal SES (measured via education) & smoking, seasonality

	USFS BlueSky framework and Georgia Forestry Commission + $PM_{2.5}$ ambient monitoring station data from US EPA AirData network, exposure assigned by location	
(Jones & McDermott, 2021)	Wildfire perimeter data from USGS GeoMAC system, exposure assigned by location	Maternal SES (measured via education) & smoking, seasonality, county & state of birth
(J. Li et al., 2021)	GEO-chem model with data from MERRA-2 & CEDS + satellite-based $PM_{2.5}$ estimates, exposure assigned by location	Non-fire-sourced $PM_{2.5}$, ambient temperature/humidity; sibling-match to control for non-measured confounders (e.g. genetics, maternal SES, access to medical services; sibling)
(O'Donnell & Behie, 2015)	Damage level to area of location of maternal residence	Maternal indigenous status, smoking, gestational diabetes

(Park et al., 2022)	Mother's primary residence zip code proximity to closest edge of wildfire	Seasonality, gestational age, regional pollution, SES
(Requia et al., 2022)	"wildfire waves" = wildfire records and $PM_{2.5}$ concentration exceeds 90^{th} percentile values for 2001-2018; exposure assigned binary case(1)/control(0) based on trimester & presence of wildfire wave	Seasonality, individual level (maternal SES, smoking, pre-existing medical conditions)
(Willson et al., 2019)	Daily monitoring at CARB-operated dedicated air quality monitoring site. Exposed = breeding season cohorts during years with high PM	Seasonality

Table 4 Overview of wildfire study designs, including smoke measurement method used and confounding variables accounted for.

FUTURE RESEARCH NEEDS

Long-term and Chronic Exposure Effects

As wildfire seasons become more frequent and severe, studies that characterize wildfire exposure as a chronic and long-term threat and study its effects in that context become increasingly imperative. Current research generally classifies wildfire smoke exposure as acute and short-term, considering only one wildfire event or one season, but a few potential long-term effects have been proposed. Two long-term effects of wildfire smoke exposure are often mentioned: impairment of immune function and carcinogenic properties of particles that are emitted during the combustion process.

Tiny particles in the smoke are able to evade the respiratory system's defenses penetrate deep into the respiratory tract and cause inflammation and cytotoxicity (Aghasafari et al., 2019; Black et al., 2017; Guyon et al., 2005; Williams et al., 2013). This leads to impairment of macrophages and cilia that comprise the respiratory, immune defense, resulting in a long-term increase in the risk of illness (Croft et al., 2020; Landguth et al., 2020; Zhu et al., 2020). For example, one study observed a correlation between smoke levels and COVID-19 cases during the peak of the COVID-19 pandemic in the summer of 2020 in British Columbia (Zhu et al., 2020), and implies that smoke exposure may be an important factor leading to an increase in the frequency of visits to healthcare providers due to respiratory symptoms brought on by the inhalation of smoke. Another study found an increase in the severity of the influenza season following a severe wildfire season, suggesting that the long-term immune impairment caused by wildfire exposure contributed to the increase in influenza cases that year (Landguth et al., 2020).

Another concern of long-term exposure to the pollutants in wildfire smoke is the increased risk of cancer. Though the composition of wildfire smoke varies by fire, many nanoparticles emitted during the combustion process are common between wildfire and biofuel fires. Many of these common particles and their components (e.g., PAHs) are known to be toxic and carcinogenic, suggesting that wildfire smoke exposure may be associated with an increased risk of developing cancer in the long term (Navarro et al., 2018). However, long-term studies observing people who were exposed to wildfires and whether they developed cancer have not been conducted, so the data to support this hypothesis has yet to be collected.

Moving into the future, it will be possible to conduct longitudinal studies of repeat wildfire exposures over many years. These types of studies can provide data regarding these proposed long-term health effects of wildfire exposure. Of particular interest are the long-term effects of prenatal wildfire smoke exposure on the child as well as the mother, which are currently unknown.

Standard Outcomes of Interest

While birth outcomes related to gestational age and birth weight are discussed in nearly every study related to pregnancy and birth outcomes, other outcomes received far less attention and were often excluded. In order to ensure these less obvious effects of wildfire smoke exposure are given ample attention and investigation, a standard list of outcomes of interest would be helpful in guiding future research. This enables a wealth of data and knowledge to accumulate around the other possible pregnancy and birth effects of wildfire exposure.

Building a standard list of outcomes of interest is informed by a variety of sources. Based on the existing wildfire exposure research, outcomes discussed in this paper that warrant further investigation include pregnancy complications such as gestational diabetes and gestational hypertensive disorders, which were only mentioned in one study, due to the significance of their association with wildfire smoke exposure (Abdo et al., 2019) and their interactions with susceptibility to wildfire smoke as well as other pregnancy and birth outcomes (Lin et al., 2015; Mistry et al., 2021; Shen et al., 2017). Moreover, similar to how PTB and LBW were the primary outcomes under investigation due to their significance in the ambient air pollution literature, other pregnancy and birth outcomes significantly associated with ambient air pollution exposure should also be considered, such as fetal mortality and congenital malformation (deSouza et al., 2022; Goyal et al., 2019; Vrijheid et al., 2011; Wang et al., 2019). Finally, it is likely that as mechanistic pathways for wildfire smoke exposure are established, they will suggest related potential outcomes to investigate, such as the ramifications of placental and endocrine disruptions, toxicity profiles of the most prevalent components of wildfire smoke, and epigenetic markers of stress.

On the practical side, a published list of pregnancy and birth outcomes will enable public health officials to communicate clearly the risks associated with wildfire exposure. Moreover, as research progresses and a knowledge base is built around these standard risks, it will also enable policymakers to make more informed decisions regarding the true risks of wildfire smoke exposure and how best to balance choices around risk mitigation.

INTERVENTION STRATEGIES

Wildfire occurrence is expected to increase as a result of climate change, so mitigating the adverse health effects of wildfire smoke exposure is of critical importance to public health officials. Three opportunities for intervention will be discussed: reducing the occurrence and severity of wildfires themselves, modifying human behavior to reduce exposure to wildfire smoke, and mitigating the effects of wildfire smoke exposure.

Land Management Strategies: Reducing Wildfire Frequency and Severity

Prescribed burning is a land management strategy aimed at reducing the severity and frequency of wildfires, which would decrease exposure to wildfires overall and consequently alleviate all adverse health effects associated with wildfire smoke. Based on the understanding of wildfire as a natural process, prescribed burns are controlled burning of areas of the forest that would have burned without fire suppression. This clears away fuel loads and gives land managers a degree of control over the severity of a future wildfire. As demonstrated in a study on mega-fires, there is a nonlinear relationship between mega-fire burn area and severity of health impacts, such that larger fires have an outsized impact on the health of affected communities (Jones & McDermott, 2021). This can help justify increased spending on prescribed burns to dampen a potential megafire as a preventative measure to avoid outsized spending on damage control later. Thinning the underbrush also frees forest floor space for new growth, ultimately restoring the health of the forest and increasing resilience to future fires.

A critical consideration for prescribed burning is whether prescribed burns, which are generally chronic and controlled, are truly safer wildfires, which are generally acute and sporadic. Prescribed burns still generate smoke plumes that affect the air quality of downwind communities, much like wildfires. Prescribed burns are more controllable in scale and fuel type and generally produce fewer emissions than wildfires (Jaffe et al., 2020); however, preliminary evidence suggests that prescribed burns may have a larger impact on health. Yet observational data on prescribed burning is quite limited, and further research is needed to deeply understand the health effects of prescribed burning in comparison to wildfire. There is a need to further investigate smoke as a chronic exposure rather than a single acute exposure in order to fully understand the health effects of wildfire smoke in comparison to prescribed burn smoke and consequently develop efficient and impactful mitigation strategies. And given that wildfires are likely to increase in frequency over time due to climate change, it is likely that people will be chronically exposed to wildfire smoke over long periods of time. This gap in knowledge also provides an opportunity for further research into strategies to lessen the health risks of prescribed burns - which factors can be controlled in order to minimize health risks?

Prescribed burning as a land management policy also faces a few obstacles. Prescribed burning hinges on the land manager's ability to control the fire, which is becoming more and more difficult as climate change increases the duration, aridity, and temperature of wildfire seasons, effectively decreasing the number of days when it is safe to light prescribed fires. Climatological trends are unlikely to change in the short term, placing pressure on land managers to implement preventative prescribed burning measures while still possible.

Even when land managers schedule a prescribed burn, they face another obstacle in trying to gain public acceptance. Community opposition to prescribed burning can affect policies that regulate the conduct of prescribed burns – as demonstrated in the Ashland Forest Resiliency Project in Oregon, overly limited local policy can severely impede the ability of prescribed burns to provide truly impactful air quality improvements. A complicating factor is the fact that while prescribed burns are regulated and implemented on the local scale, smoke plumes from prescribed burns impact large areas downwind. For example, the air quality exacerbation events in Ashland, Oregon, were primarily due to wildfires elsewhere in Oregon and Northern California, not the local Almeda fire. But policies around prescribed burning often do not take into account the health impacts on downwind communities, and it is not uncommon for a scheduled prescribed burn to be canceled due to resistance from downwind communities. Public acceptance of prescribed burning is a crucial step towards being able to run larger and more frequent prescribed burns. Improved communication and a partnership between land managers, air districts, prescribed burn managers, and the public can increase public acceptance. Informing the public of the benefits of prescribed burns - decreasing the occurrence of severe wildfire, controlling the severity, frequency, and timing of fire events, and ultimately improving overall air quality for downwind communities in the long term - can help encourage public acceptance as well. Increasing public awareness of the location and timing of prescribed burns also sets expectations and provides an opportunity for people to appropriately prepare for air quality exacerbation events, reducing exposure and increasing public acceptance of the practice.

Another obstacle for the implementation of prescribed burns is the diminishing pool of personnel able to carry out the prescribed burns - wildland firefighters. As front-line workers, wildland firefighters are among the most susceptible to the health risks of wildfire smoke. They do not have the option to take shelter and must perform high exertion work in $PM_{2.5}$ levels around 300µg/m^3, often in extreme heat and humidity, for 8+ hours. In such extreme conditions, basic personal protective equipment such as N-95s are not effective protection, and heavy-duty respirators are not suitable options for such high-intensity work (Adetona et al., 2016). Smoke exposure on the front-line is also more complex than for the average person: in addition to respiratory inhalation of smoke particles, they also come in contact with smoke particles via the cutaneous route. Furthermore, wildland firefighters often disturb the soil and release crystal & silica dust into the air, adding to the hazardous elements of air pollution they are exposed to (Adetona et al., 2016).

As expected in such extreme working conditions, wildland firefighters experience an increased rate of acute physiological response, on-the-job cardiac events, and on-the-job stroke (Adetona et al., 2016). There is a higher rate of kidney disease among agricultural workers in hot environments, demonstrating the compounding effect of the additional stressor of extreme heat on the development of adverse health outcomes (Johnson et al., 2019). The long-term effects of occupational wildfire exposure among wildland firefighters include increased mortality due to lung cancer and cardiovascular disease (Navarro et al., 2019), hypertension, and elevated cholesterol (Semmens et al., 2016a), and cross-seasonal adverse changes in cardiometabolic measures (Coker et al., 2019). Ultimately, these direct adverse health effects and their downstream consequences reduce the quality of life, motivation to continue working, and productivity. Attrition of the wildland firefighter workforce will significantly impede the opportunity for improvement that prescribed burning presents. However, prescribed burns provide a controlled environment for those exposures to occur and lessen the burden of uncontrolled wildfires. Educating the workforce on the safe implementation of prescribed burns and methods to reduce their exposure to wildfires is critical to protecting their health.

Public Health Tools: Reducing Exposure

Public health tools are a valuable and cost-effective resource for protecting people from the health effects of wildfire smoke. Ideally, public health strategies are data-driven and optimize effectiveness, sustainability, and equitability. Public health tools include the use of communication, such as outlooks, advisories, and responding to inquiries; intervention, such as air shelters, provision of portable air filters & masks; and policy, by canceling or postponing events, closing schools, and setting up safeguards.

Each of these means of protecting people requires a clear picture of current air quality conditions and future air quality forecasts - this necessitates improvements in monitoring & forecasting abilities, with details on timing, intensity, and duration of air quality events prioritized over accuracy/complexity. This can be achieved by increasing the amount and availability of low-cost measurement devices, which would increase access for under-served populations and thus provide information to more people.

Potential avenues for effective communication that leads to changes in behavior are through healthcare providers & insurance companies (smoke action plan/eMR, education/clinic materials). Another possibility is through the integration of air quality forecasts into regular weather forecasts, which are easily accessible, regularly checked, and widely understood. However, the visual perception of smoke versus metrics such as AQI can sometimes be at odds and create dissonance; choosing an index that better matches public perception can improve confidence in measurement tools. Knowledge of current and future air quality conditions encourages and empowers people to plan around smoke more appropriately. For information to flow from meteorological forecasts to advisories and action plans, a partnership between atmospheric scientists and public health officials is critical (e.g., avoiding exposure, early warning, changing resistance to prescribed burns).

Armed with accurate projections of air quality events, public health officials require clear answers to health questions in order to balance risks. Yet the greatest gap in knowledge is in a comprehensive understanding of the full extent of the health effects of $PM_{2.5}$ components in wildfire smoke. This review walks through the health risks surrounding pregnancy and birth outcomes related to wildfire smoke exposure; similar studies for body systems, different age groups, and different subpopulations are needed in order to create a full picture of the potential health risks.

Investing in preparative and preventative measures such as medication/disease management and air filters can be much more accessible and effective for people with fewer resources when compared to recovering from or dealing with the consequent health effects of wildfire smoke exposure. Staying indoors is often recommended as a measure to protect people from smoke exposure. However, the effectiveness of staying indoors depends greatly on how well indoor air quality is protected from outside air pollution. Indoor air quality sensors inform the status of the air quality, masking and limiting outdoor time can protect individuals from exposure to particles in the air, and air conditioning and HEPA filters can provide relatively simple and low-cost solutions to improving the air quality (Holm et al., 2021). On a policy level, prioritizing smoke readiness through assessment of wildfire risk when new housing developments are built and integrating seasonal power shut-offs to reduce wildfire ignitions can systematically reduce the occurrence of and exposure to wildfire smoke (Aguilera et al., 2020).

Vulnerable Populations

Wildfire smoke has dramatically different effects on people due to disparities in exposure, health responses, and options to adapt. Accessibility and clarity of communication are especially important for reaching groups most at-risk from smoke exposure, which includes people with pre-existing related conditions, people of low socioeconomic status (SES), children and the elderly. Allocating resources to target populations most at-risk is the most cost-effective strategy for reducing adverse outcomes for the population.

People with pre-existing conditions are more likely to suffer more severe adverse health outcomes due to wildfire smoke exposure (Vicedo-Cabrera et al., 2016). The combined stressors of disease and acute smoke exposure lead to compounding of adverse health effects. In addition, wildfire smoke exposure frequently occurs with other environmental stressors, such as extreme heat or disease, as was the case with COVID-19 during the 2020 and 2021 wildfire seasons (Zhu et al., 2020). These further exacerbate the vulnerability of populations with pre-existing conditions and compound the adverse health outcomes associated with wildfire smoke exposure.

Due to the increasing cost of living in large cities, groups of low SES are pushed to relocate into more affordable housing developments. Many of these are located at the wildland-urban interface (WUI), placing dwellings in significant danger of wildfire damage and these people at significantly increased risk of wildfire exposure – a 2020 study found that 13 million people living with extreme fire risk are socially vulnerable Americans (Davies et al., 2018; Mietkiewicz et al., 2020). In addition, people of low socio-economic status frequently do not have access to information and resources that would help protect them from wildfire exposure. Crucial resources such as information exchanged via electronic & social media, air shelters and air filters are less accessible. As schools close, those who rely on schools for air-shelter lose that protection. To exacerbate the situation, due to the momentum of worsening wildfire seasons, these people will experience increased risk and exposure to wildfire over time.

Different biophysical responses to wildfire smoke at different stages of development place children and the elderly especially at risk. Thus, it is necessary to devote resources to studying specifically the developing respiratory and immune systems of pediatric populations and the weakened respiratory and immune systems of geriatric populations. Existing studies provide evidence that wildfire smoke especially affects the respiratory health of the elderly (Castro et al., 2009; Liu, Wilson, Mickley, Ebisu, et al., 2017), and increases the rate of asthma and rhinitis among children (Holm et al., 2021; Stowell et al., 2019). Critical to the protection of children from exposure to wildfire smoke is partnership between public health officials and school administrators, exchanging information about how to reduce exposure.

Treatment Tools: Mitigating the Health Effects

Due to the unknown nature of the mechanism behind wildfire smoke exposure leading to its adverse health effects, medical interventions specific to treating wildfire smoke exposure were not found. Elucidation of the physiological mechanisms through which wildfire smoke causes adverse health outcomes will greatly aid in the development of medical interventions to prevent them. At present, the symptoms due to adverse health effects associated with wildfire smoke exposure are likely treated by the standard of care.

Studies that attempt to counter the adverse psychological effects of wildfire exposure show very little effectiveness. A study of maternal mental health after the Fort McMurray Wood Buffalo wildfire showed that an expressive writing intervention aimed at improving maternal mental health after the fire were ineffective; psychological resilience was indirectly related to the incidence of peritraumatic distress and post-traumatic stress symptoms, moderated by satisfaction with their social support network (Verstraeten et al., 2021). The lack of effective tools to combat the negative effects of wildfire smoke exposure emphasizes the need to implement preventative measures early and effectively.

CONCLUSION

Wildfires pose a growing threat to population health and safety due to projected increases in frequency and severity in the future. A comprehensive understanding of their health effects, especially on vulnerable populations such as pregnant women, is essential to developing effective, sustainable, and equitable policies for land management and public health. This narrative review summarized findings from the existing body of research concerning wildfire smoke exposure during pregnancy and the associated adverse pregnancy and birth outcomes evaluated points of inconsistency that require reconciliation and delved into the practical considerations of implementing these studies into land management and public health policy.

While research has been published specifically on the adverse maternal and birth outcomes associated with wildfire smoke, the knowledge base is still small and underdeveloped. There is significant evidence to support the association of prenatal wildfire smoke exposure with birth outcomes such as preterm birth and low birth weight; for other birth outcomes, such as fetal mortality and congenital malformation, and pregnancy complications, such as gestational hypertensive disorders and gestational diabetes, the evidence is weak or mixed, suggesting a potential association or deeper investigation to understand the nuances of the association. It is likely that wildfire smoke affects maternal and prenatal health through a variety of etiologic pathways, several of which are presented in this paper. Elucidating the mechanisms of precisely how wildfire smoke exposure leads to adverse pregnancy and birth outcomes will not only inform public health guidance and medical care for people affected by wildfire smoke but also cast light on important topics for further research such as the psychological effects and the long-term health effects of prenatal wildfire smoke exposure.

A notable shortcoming in the literature is the lack of cohesion across studies in methods and goals, which creates an obstacle for comparing data and results between studies. This is due in part to the nature of wildfires being spontaneous in location, size, and timing; yet there is still capacity for increased collaboration and standardization across studies, specifically in best practices for exposure assessment, a standard list of confounding factors to account for, and a standard list of health outcomes of interest to investigate.

When it comes to proactive measures to counteract the negative effects of wildfire smoke, it appears that while land management and public health officials are advocates of the research, implementation and policy development are still in their early stages. For both land managers and public health officials, establishing effective communication channels and methods of engaging the public is a vital step for enacting interventions that are effective and sustainable. In addition, special care must be taken for people at higher exposure and risk of adverse outcomes, such as wildland firefighters, pregnant women, and other people with vulnerable physiological and/or socioeconomic status.

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