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Associations between wildfire smoke exposure during pregnancy and risk of preterm birth in California

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ABSTRACT

There is limited population-scale evidence on the burden of exposure to wildfire smoke during pregnancy and its impacts on birth outcomes. In order to investigate this relationship, data on every singleton birth in California 2006–2012 were combined with satellite-based estimates of wildfire smoke plume boundaries and high-resolution gridded estimates of surface PM_{2.5} concentrations and a regression model was used to estimate associations with preterm birth risk. Results suggest that each additional day of exposure to any wildfire smoke during pregnancy was associated with an 0.49 % (95 % CI: 0.41–0.59 %) increase in risk of preterm birth (<37 weeks). At sample median smoke exposure (7 days) this translated to a 3.4 % increase in risk, relative to an unexposed mother. Estimates by trimester suggest stronger associations with exposure later in pregnancy and estimates by smoke intensity indicate that observed associations were driven by higher intensity smoke-days. Exposure to low intensity smoke-days had no association with preterm birth while an additional medium (smoke PM_{2.5} 5–10 µg/m³) or high (smoke PM_{2.5} > 10 µg/m³) intensity smoke-day was associated with an 0.95 % (95 % CI: 0.47–1.42 %) and 0.82 % (95 % CI: 0.41–1.24 %) increase in preterm risk, respectively. In contrast to previous findings for other pollution types, neither exposure to smoke nor the relative impact of smoke on preterm birth differed by race/ethnicity or income in our sample. However, impacts differed greatly by baseline smoke exposure, with mothers in regions with infrequent smoke exposure experiencing substantially larger impacts from an additional smoke-day than mothers in regions where smoke is more common. We estimate 6,974 (95 % CI: 5,513–8,437) excess preterm births attributable to wildfire smoke exposure 2007–2012, accounting for 3.7 % of observed preterm births during this period. Our findings have important implications for understanding the costs of growing wildfire smoke exposure, and for understanding the benefits of smoke mitigation measures.

1. Introduction

Exposure to poor air quality has been associated with a wide range of adverse health outcomes in a variety of settings (Atkinson et al., 2014; Feng et al., 2016). However, the level of individual vulnerability can vary dramatically across the general population (Deryugina et al., 2019). One group thought to be particularly vulnerable is young children. Even prior to birth, fetal health can be affected by particulate matter both through direct transplacental exposure and indirectly through induced changes in maternal health (Glinianaia et al., 2004; Klepac et al., 2018). Recent reviews (Klepac et al., 2018; Bai et al., 2020; Bekkar et al., 2020; Lamichhane et al., 2015) highlighted evidence of an

association between exposure to particulate matter during pregnancy and elevated risk of preterm birth, defined here as a birth prior to the 37th week of pregnancy.

While most past studies examining the relationship between air pollution and birth outcomes have examined exposure to total particulate matter with diameter < 2.5 µm (PM_{2.5}), the source and composition of this PM_{2.5} is changing across much of the US, with declines in emissions from transportation and power generation being increasingly offset by increased emissions from wildfires (Burke et al., 2021; O'Dell et al., 2019; McClure and Jaffe, 2018). This is particularly true in the Western US, where recent estimates suggest that wildfire smoke accounts for more than 40 % of total PM_{2.5} exposure in high fire years

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(Burke et al., 2021). Wildfire smoke is generated from the combustion of wood, other biomass sources, and in some cases, non-natural materials the fires consumes. While combustion of substances like households chemicals may be especially damaging to health, even combustion of natural biomass material generates smoke that contains thousands of chemicals, many of which adversely affect human health (Naeher et al., 2007). Indeed, existing evidence suggests that like other sources of PM_{2.5}, non-occupational exposure to wildfire smoke PM_{2.5} is associated with negative health outcomes (Liu et al., 2015; Reid et al., 2016; Cascio, 2018; Kondo et al., 2019; Borchers Arriagada et al., 2019; Amjad et al., 2021). In fact, there is some evidence that exposure to particulate matter from wildfire smoke may be even worse for health than exposure to particulate matter from other sources (Wegesser et al., 2009; Aguilera et al., 2021). Given the changing relative contribution of PM_{2.5} sources and wildfire smoke's documented harmful health effects, the extent to which wildfire smoke affects birth outcomes is an increasingly important policy question.

A recent review (Amjad et al., 2021) assessed that while the body of evidence is limited, existing work does support an association between wildfire smoke exposure during pregnancy and adverse birth outcomes. However, most previous work focused on birth weight. The review called for additional research to better understand the effects of wildfire smoke on preterm birth, the importance of exposure timing, and to identify which mothers are most vulnerable to these impacts. Our work aims to contribute to improved understanding in each of these areas. An additional motivation for this paper is that most earlier studies of adverse pregnancy outcomes from wildfire smoke were limited to small geographical extents and coarse measurements of exposure within a limited study area for a single fire season (Holstius et al., 2012; Breton et al., 2011; O'Donnell and Behie, 2013). Recent methodological advances and the availability of an increasingly long time-series of remotely sensed smoke plume measures have made exposure assessments on large populations feasible. Our study leverages these advances combined with a modeling framework designed to isolate the effect of wildfire smoke from other factors in order to improve understanding of how wildfire smoke affects preterm birth.

Our study is complimentary to recent work that utilized similar data to estimate associations between wildfire smoke and birth outcomes in Colorado (Abdo et al., 2019). However, there are several differences between our study and the previous work that allow us to provide new insights. First, by comparing within zip-code changes over time in smoke exposure and outcomes after controlling flexibly for common time trending changes in exposure and outcomes, our modeling approach is designed to isolate variation in smoke exposure from other factors that co-vary over space or time – a key step for understanding the potentially causal relationship between pollution and health (Dominici et al., 2014). Second, the changes in air quality from wildfire smoke in our sample are substantially larger than in previous studies. This is because a significant portion of smoke exposure in Colorado is due to long range transport from wildfires in the Pacific Northwest and Canada (Abdo et al., 2019) whereas the vast majority of smoke exposure in California is from active wildfires nearby. Moreover, health effects associated with smoke from local and remote fire sources may differ even for a fixed level of exposure due to differential behavioral responses when fires are far away or changes in chemical composition as smoke travels further from the source fire (Magzamen et al., 2021). Third, baseline pollution exposures vary widely across California, allowing us to examine the interaction between wildfire smoke and baseline exposure. Finally, our birth sample covers a broad range of demographics allowing us to estimate heterogeneity in effects across race/ethnicity and income. Collectively, these features allow us to make a contribution to improved understanding of impacts on the populations most likely to be vulnerable to health damages from wildfire smoke exposure.

2. Methods

Study Population - Data on birth outcomes were drawn from birth certificates in Vital Records from the Department of Health in California. The initial sample included all 3,494,256 singleton births in California occurring between January 1, 2006 and December 31, 2011. The study population was then limited to infants born between gestational ages of 23 and 41 weeks leaving a sample of 3,493,242 births. In order to avoid fixed-cohort bias (Barnett, 2011) we further limited the study population based on estimated conception date. Namely all births with conception dates prior to 23 weeks before October 2006 or after 41 weeks before December 31, 2012 were omitted leaving us with an eligible sample of 3,063,672 births. By limiting the study sample in this way, we ensured that shorter pregnancies were not under-represented early and longer-pregnancies were not over-represented later in the study period.

Following a large literature, we then used data on gestational age in weeks to construct binary variables indicating whether a birth was preterm, using different cutoffs common in the literature (gestational age < 37, 32, or 28 weeks). Mother and child characteristics linked to the birth certificate data included mother's age, mother's race/ethnicity, mother's education, mother's location of birth (foreign/domestic), parity, child's gestational age, and child's sex. Births were geolocated to the mother's 5-digit zip code of residence. We matched these data to community level income data from the American Community Survey 5-year averages (2007–2011). Median income was reported at the census tract level and was estimated for each zip-code by taking the average of overlapping census tracts weighting by the area of overlap. After accounting for missing values in the covariates, the sample of complete observations included 3,002,014 births (Table 1).

This work was approved by the Stanford University Institutional Review Board and the California State Committee for the Protection of Human Subjects.

Exposure data - Smoke plume extents were assembled from NOAA's Hazard Mapping System (HMS) Fire and Smoke Product (Schroeder et al., 2008) (Fig. 1). The HMS produces daily lists of active fires and polygons of smoke plume boundaries. The plume boundaries are hand drawn by trained analysts using animated visible channel imagery primarily from the geostationary operational environmental satellite system (GOES). The system provides a measure of smoke and fire activity every few hours throughout the daytime across the entire US for more than a decade. A limitation of these data is that they are unable to detect smoke plumes obscured by cloud cover or plumes at night. They are also unable to identify the vertical height of plumes and therefore cannot easily distinguish between plumes at surface level and plumes high above the ground.

In order to assess the extent to which plumes affected surface conditions, we combined plume boundaries with recently released daily 1 × 1 km gridded estimates of surface PM_{2.5} concentrations across the United States (Di et al., 2021; Di et al., 2019). These data are one of an increasing number of high temporally and spatially resolved estimates of surface PM_{2.5} concentrations (Di et al., 2021; Reid et al., 2021; Park et al., 2020; Hu et al., 2017) that have been developed using machine learning algorithms to incorporate a variety of inputs including ground monitor data, satellite observations, chemical transport model predictions, and other features. Among the available high-resolution daily PM_{2.5} products we chose the only one that is available for all of our study years.

Exposure assessment - Smoke exposures were assigned to individual pregnancies at the zip-code level. Births from mothers with mailing address zip-codes that corresponded to P.O. boxes were dropped from the sample because we could not identify residence locations to assign exposures. This accounted for the loss of 7,033 births from the sample (0.2 % of eligible births, see Table 1 for details). Exposure to wildfire smoke was first characterized by counting the number of days in a given period that smoke plumes from the HMS data product intersected with

Table 1
Study population characteristics by pregnancy length.

	Gestational Length				All pregnancies
	20–27 weeks	28–31 weeks	32–36 weeks	37–41 weeks	
Eligible Analysis Sample (N)	10,021	18,494	191,225	2,843,932	3,063,672
Share Sample (%)	0.3	0.6	6.2	92.8	100
Child Sex (% female)	45.2	44.8	45.0	49.1	48.8
Missing (%)	0	0	0	0	0
Mother's Age	28.1	28.6	28.6	28.2	28.2
Missing (%)	0	0	0	0	0
Mother's Race/Ethnicity	49.6	50.0	49.4	48.9	48.9
Hispanic (%)					
Non-Hispanic Asian (%)	9.8	11.8	13.0	12.8	12.8
Non-Hispanic White (%)	19.7	21.0	24.3	27.7	27.4
Non-Hispanic Black (%)	14.7	11.1	7.8	5.7	5.9
Missing (%)	2.5	2.6	2.0	1.8	1.8
Temperature (C)	17.4	17.3	17.2	17.0	17.0
Missing (%)	0	0	0	0	0
Wildfire smoke exposure (days)	8.6	8.8	8.8	8.6	8.6
Missing (%)	0.3	0.3	0.2	0.2	0.2
Non-Missing Sample (N)	9,739	17,960	187,004	2,787,311	3,002,014
Share Sample (%)	0.3	0.6	6.2	92.8	100
^a 3rd Trimester Sample (N)	–	6,083	187,004	2,787,311	2,980,398
Other Analysis Covariates	58.7	60.1	61.3	62.9	62.8
Income (\$1,000)					
Missing (%)	1.4	1.3	1.4	1.4	1.4
Smoked cigarettes (%)	0.5	0.5	0.5	0.3	0.3
Missing (%)	11.4	10.7	8.7	4.7	5.0

^a The sample for analyses that included 3rd trimester exposure (measured as 4 weeks prior to birth) was limited to births occurring week 31 or later (i.e., 4 weeks into third trimester) to ensure opportunity of exposure did not vary with gestation length. The 28–31 week gestation length category that included 3rd trimester exposure therefore only included week 31 births.

any part of the zip code (referred to as “smoke-days”). Across our sample there were 24 days (< 1 %) where all smoke plume information was missing due to cloud cover. When smoke plume observations were missing we assumed that smoke was not present. This smoke-day metric provided a count of the number of days in all or part of the gestational period with any type of exposure to wildfire smoke. We treat this as our primary smoke exposure measure.

While counts of smoke-days provide a measure of accumulated smoke exposure during a pregnancy, they do not contain information on exposure intensity, as plumes can vary in their density. An optimal intensity metric would measure the amount of PM_{2.5} or other pollutants that come directly from wildfire smoke. However, separating smoke PM_{2.5} from other PM_{2.5} is empirically challenging. A number of modeling approaches have been developed to address this challenge, including the use of chemical transport models (CTMs) (O'Dell et al., 2019; Fann et al., 2018; Wilkins et al., 2018). CTMs in principle allow direct linking of emissions sources (such as wildfires) to pollution concentrations, but are challenging to implement in our setting for multiple reasons. In particular, recent studies show that large uncertainties in wildfire emissions inventories can lead to many-fold differences in surface-level wildfire-attributed PM_{2.5} concentrations across the United States (and even larger regional differences in high fire years) when

different inventories are used as input to the same CTM (Koplitz et al., 2018; Carter et al., 2020).

These uncertainties are amplified by difficulties in accurately capturing plume injection heights in these models and in accurately representing the atmospheric chemistry relevant to wildfire smoke evolution (Kahn et al., 2008; Tomaz et al., 2018; Gunsch et al., 2018).

Rather than use a CTM, we instead built on recent statistical approaches (Burke et al., 2021; O'Dell et al., 2019) that combine ground-based measures of total PM_{2.5} with satellite-based measures of the timing and location of wildfire smoke plume movements. The central idea of our approach is that PM_{2.5} anomalies in a given location, defined as deviations from site- and month-specific average PM_{2.5}, can plausibly be attributed to smoke if there is a smoke plume overhead. We generated PM_{2.5} anomalies using recent high-resolution daily estimates of total PM_{2.5} (Di et al., 2019), with grid cell anomalies calculated as the difference between the grid cell-day PM_{2.5} estimate and the grid cell's ‘background PM_{2.5}’ where background PM_{2.5} was the month-of-year average PM_{2.5} for that grid cell on non-smoke days across all years in the sample. Any positive anomaly from this background level was then attributed to smoke if there was a plume overlapping the grid cell on that day.

To then combine this intensity information with the duration information captured in our primary smoke-day measures, we calculated accumulated exposure to different smoke intensities by assigning smoke days to different intensity bins. Smoke-days with PM_{2.5} anomalies < 5 µg/m³ were assigned low intensity, smoke-days with PM_{2.5} anomalies of 5–10 µg/m³ were assigned medium intensity, and smoke-days with PM_{2.5} anomalies > 10 µg/m³ were assigned high intensity; as 5 µg/m³ and 10 µg/m³ were the median and 75 % of the estimated smoke PM_{2.5} distribution, this corresponded to bins at 0-50th, 50-75th, and > 75th percentiles of smoke PM_{2.5}. Grid cell level bin counts were then aggregated to the zip-code day level by taking averages of bin counts across grid cells in each zip code.

Finally, daily zip code smoke exposures for any smoke and by intensity were summed to weekly exposures, matched to week of pregnancy, and summed across defined exposure periods (i.e., trimesters or full pregnancy).

Exposure was assessed for each trimester with periods defined by week relative to estimated conception date. Trimester 1 was defined as weeks 1–13 following conception, Trimester 2 was defined as weeks 14–26, and Trimester 3 exposure was defined as the last four weeks of pregnancy so that the opportunity of exposure did not vary with gestation length. Third trimester exposure was not assessed for births prior to week 31 so as to avoid overlapping trimester exposure periods. Total pregnancy exposure was modeled as the period across the three trimesters as defined above.

Impacts of exposure to wildfire smoke - Associations between pre-term births of varying severities (< 37, 32, or 28 weeks) and exposures were estimated using multiple regression models. In order to isolate variation in smoke exposure from other time-invariant or time-varying factors that might be correlated with both smoke exposure and risk of PTB, we utilized repeated observation of birth outcomes across many zip codes and over time. In particular, our regression analysis included dummies (fixed effects) for each zip-code-month (i.e. 12 dummies for each month of the year in each of the 2,610 zip codes) as well as for each county-year (i.e. 7 dummies for each of the years in each of the 59 counties). Inclusion of these fixed effects meant that resulting associations between smoke exposure and PTB were estimated by comparing birth outcomes within zip codes over time as smoke exposure fluctuated, after accounting for any common trends in either smoke exposure or PTB across zip codes in the same county – e.g. June 2010 versus June 2009 in zip code 94305, after accounting for any differences between 2010 and 2009 in the surrounding county. This approach flexibly accounted for all time-invariant differences between zip codes in either PTB or smoke exposure, regardless of whether they're directly measured, and for local trends over time in either PTB or smoke exposure. In total, 23,202 zip

a Data example: Smoke and fire on Jun 17, 2008 **b** Average number of smoke days per year **c** Average all source PM_{2.5}

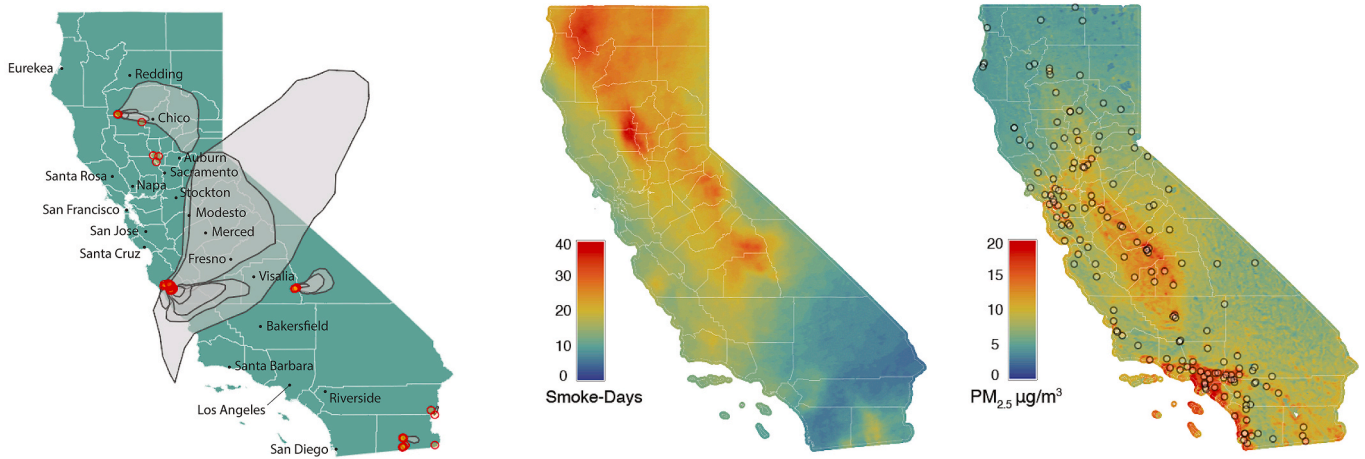


Fig. 1. Spatial patterns of smoke and all-source PM_{2.5} exposure. **a.** An example of the daily remotely sensed smoke and fire data showing smoke plumes and active fires on June 17, 2008 when several fires burned simultaneously across the state. **b.** The average number of days exposed to wildfire smoke per year. **c.** Average PM_{2.5} levels (Van Donkelaar et al., 2016).

code by month dummies and 441 county by year dummies were included in the regressions.

We also included birth- and mother-level covariates known to influence the risk of preterm birth, including mother’s age and mother’s age squared, dummy variables for mother’s completion of high school, mother’s completion of at least some college, mother’s race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, Hispanic), for whether the mother was foreign born, and for the child’s sex. These covariates, most of which influence the risk of preterm birth but may or may not be correlated with wildfire smoke exposure, served to add precision to our estimates by explaining a portion of the variation in preterm birth risk. Results are shown both with and without these adjustments.

We estimated the impact of smoke on preterm birth split by trimester or across the entire pregnancy and for total smoke or by smoke intensity:

$$y_{izcmy} = \beta_1 smoke_{zcmym}^{tr1} + \beta_2 smoke_{zcmym}^{tr2} + \beta_3 smoke_{zcmym}^{tr3} + \theta X_{izc} + \alpha_{zm} + \gamma_{cy} + \epsilon_{izcmy} \tag{1}$$

where y was a dummy for preterm birth for child i with mother residing in zip-code z and county c in month m and year y . $smoke^{tri}$ indicated the count of smoke-days in the respective trimester (or alternatively the three smoke trimester measures were replaced by a single pregnancy measure). X included child and mother covariates, α was a set of zip by month dummies, γ was a set of county by year dummies, and ϵ was our error term. β in Equation (1) measured the total effect of smoke exposure during the relevant exposure period – which may include smoke-derived PM_{2.5} as well as other non-PM_{2.5} components of smoke – on preterm birth. For the smoke intensity regressions each of the smoke-day counts ($smoke$ in equation (1)) was replaced with multiple variables each counting the number of smoke-days of a given intensity.

We did not include temperature, humidity, or other weather variables as controls in the main analysis, because these variables can drive variation in fire activity and thus smoke exposure. Therefore, controlling for them would inappropriately absorb variation in the main exposure of interest. However, because it’s plausible that these variables could have effects on birth outcomes that are independent of their effects on fire and smoke, in robustness checks we did control for these variables.

Heterogeneity Analysis - Given existing evidence that different racial and socioeconomic groups could be both differentially exposed to and differentially affected by air pollutants, we also modeled differential effects by income group, mother’s race/ethnicity, and baseline smoke

exposure. For each case we interacted smoke exposure with dummy variables indicating whether the child was in the sub-group category (Eq. (2)). For tractability interaction models were not estimated separately by smoke intensity or separately by trimester.

$$y_{izcmy} = \beta_j \left(smoke_{zcmym}^{preg} \cdot \sum_{j=1}^n Z_{jzc} \right) + \alpha \left(smoke_{zcmym}^{preg} \right) + \omega_j \sum_{j=1}^n Z_{jzc} + \theta X_{izc} + \alpha_{zm} + \gamma_{cy} + \epsilon_{izcmy} \tag{2}$$

While mother’s race/ethnicity was an individual level covariate, income and baseline smoke exposure were averages in the mother’s zip-code of residence. We tested whether coefficients estimated for each sub group were statistically different from zero as well as whether they were statistically different from each other, both in terms of relative impacts (percentage change in preterm birth risk above group-specific baseline) and absolute impacts (change in preterm birth risk). Relative and absolute impacts might differ, as baseline risk of preterm birth differs by race and income in CA (Fig. 2).

Attribution Estimate - Finally, we used our smoke-days regression model to estimate the number and share of preterm births attributable to smoke each year. The number of attributable preterm births was estimated each year in each zip code by first multiplying the number of smoke days by $\hat{\beta}$ in the full pregnancy exposure version of Equation (1) to generate an estimate for the change in probability of a preterm birth in that zip-code and year. This change in probability was then multiplied by the number of observed births in that zip-code and year to generate an estimate for the number of preterm births attributable to smoke. Finally shares of preterm births attributable to smoke were calculated by dividing the number of predicted preterm births by the number of observed preterm births in that zip-code and year. These estimates are reflective of singleton births that occurred in California during this period but do not include additional preterm births associated with multiple births.

Estimation Procedures - Our preferred specification for the regression models described in Equations (1) and (2) was a linear probability model (LPM) estimated with OLS. While LPM can be biased for binary dependent variables (Horrace and Oaxaca, 2006), nonlinear models (eg logit) can be biased in short panels with fixed effects (Heiss et al., 2019), which is our setting. LPM also offer more interpretable results over common non-linear alternatives, with parameter estimates directly interpretable as marginal effects (i.e., change in the outcome per unit of exposure); unlike odds or risk ratios, these marginal effects are also

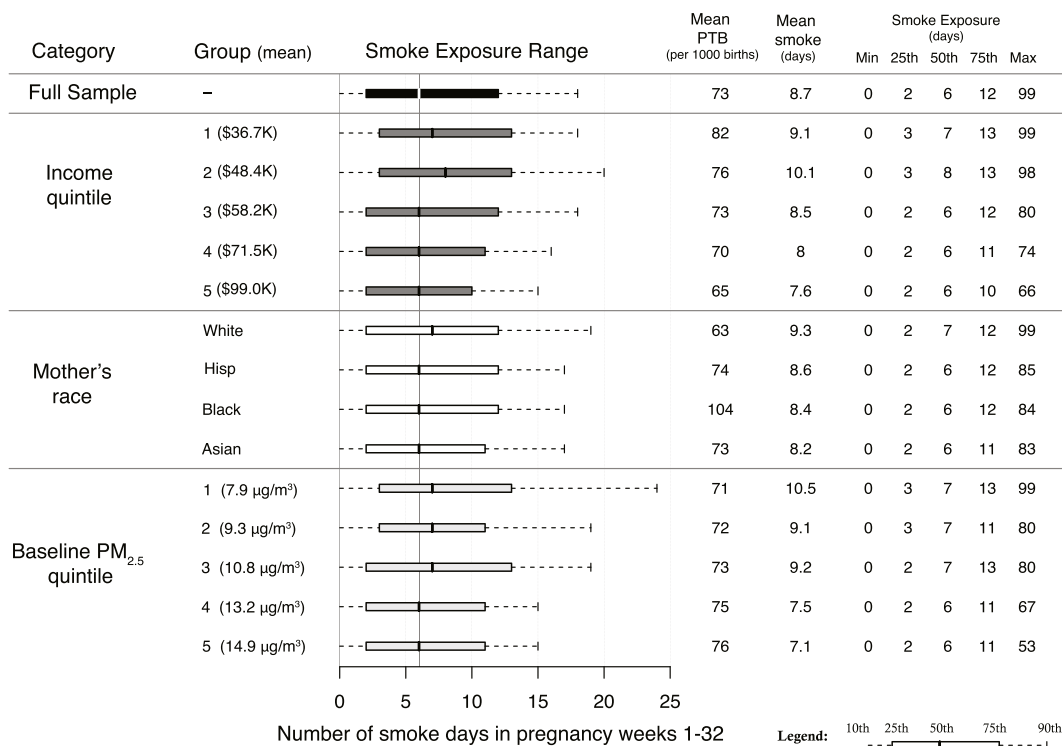


Fig. 2. Heterogeneity in smoke exposure. Each row shows the distribution of smoke exposure for a different group. The first row shows the full sample and subsequent rows show exposure for different subgroups. Righthand side columns show mean preterm birth rate (< 37 week), smoke exposure (smoke-days per pregnancy), and quantiles of smoke exposure.

directly comparable across studies when presented in absolute terms because they are not relative to an in-sample sub-group. Estimating an LPM therefore allowed us to report both relative and absolute coefficient estimates. LPMs are most problematic when used for predictions (because predictions can fall outside of the 0,1 interval) which we avoided here. Nonetheless, in order to ensure results were not dependent on the use of an LPM, we also estimated the main specifications with a logit model which allowed us to present results as Odds Ratios. Results from OLS estimation are presented in the main text and results from logit estimation are presented in the supplement. Estimation of both OLS and logit models was carried out using the fixest package (0.4.1) in the R programming language (3.5.3).

3. Results

Sample Overview - Our analysis included data on 3,002,014 births occurring in California between 2006 and 2011. Overall, 9,739 (0.3 %) births in our sample occurred prior to week 28 while 17,960 (0.6 %) occurred weeks 28–31 and 187,004 (6.2 %) occurred from weeks 32–36 (Table 1). 2,787,311 (92.8 %) births in our sample were full term (> 36 weeks). Approximately half of the mothers in our sample were Hispanic, one-quarter were non-Hispanic White, and the other quarter were split between non-Hispanic Asian, Black, and other. Community-level median household income in our sample zip-codes was about \$63,000.

Exposure Assessment - Fig. 1 illustrates the exposure data. Spatial patterns of average smoke-days per year (Fig. 1b) and total PM_{2.5} concentrations (Fig. 1c) differed visually across zip codes, consistent with the local importance of non-wildfire sources of PM_{2.5} in some areas but not others. Indeed, a naive regression of sample average PM_{2.5} concentrations on the average number of smoke days in each zip code suggests that each additional smoke day was associated with 0.62 µg/m³ (p = 0.042) lower average PM_{2.5} concentration (Fig. S1a). This association demonstrates the importance of non-wildfire sources of pollution in total PM_{2.5} concentrations in CA, and highlights the difficulty in using

cross-sectional comparisons to quantify smoke impacts on health.

To understand the temporal relationship between smoke exposure and PM_{2.5} concentrations – the variation we exploit to estimate health impacts – we regressed a time series of monthly zip code PM_{2.5} concentrations on the number of smoke days in that month. In contrast to the cross-sectional relationship, we found that each additional smoke day above zip-code specific averages in the panel relationship was associated with 0.44 µg/m³ (p < 0.01) higher PM_{2.5} concentration in that month (Fig. S1b). Therefore, while baseline averages of smoke and PM_{2.5} were negatively correlated over space, deviations from these averages were positively correlated over time. These findings provide evidence that our smoke metric explains relevant temporal variation in pollution exposure across our study locations.

The cross-sectional spatial patterns discussed above suggest a differing exposure burden for wildfire smoke than for total (all-source) PM_{2.5} across population sub-groups, and examining exposures across the intersection of income and race indeed revealed contrasting exposures (Fig. 2 and Fig. S2). Across racial and ethnic groups, mothers residing in higher income zip-codes were exposed to lower average PM_{2.5} concentrations than mothers residing in lower income zip-codes. There were also differences across race/ethnicity: Non-White mothers residing in zip-codes with below-median income were exposed to substantially higher average total PM_{2.5} than White mothers in the same income deciles. However, this relationship was the opposite for smoke: White mothers living in zip-codes in the bottom 40 percentile of income were exposed to nearly 50 % more smoke on average than Black or Asian mothers in any of the lowest income deciles. Moreover, across race/ethnicity mothers residing in the highest income zip codes were exposed to moderate levels of smoke whereas mothers in these income groups were universally exposed to the lowest average levels of total PM_{2.5}. These patterns are broadly consistent with California demographics where rural zip codes close to most source fires are disproportionately White and lower income while total PM_{2.5} most affects non-White urban communities and Hispanic populations in the Central Valley.

Main Results - Estimating Equation (1) with a linear probability model, we estimated that each additional day of exposure to any wildfire smoke across the entire pregnancy was associated with a 0.49 % (95 % CI: 0.41–0.59 %) increase in the risk of preterm birth (< 37 weeks). Relative to no exposure, this translated to a predicted 3.4 % increase in preterm births at median wildfire smoke exposure frequency (7 days). Effects were largest for smoke days that occurred during the second trimester (Fig. 3a, Fig. S5 top panel). An additional day of smoke exposure during this trimester was associated with an 0.83 % (95 % CI: 0.71–0.96 %) increase in the risk of a preterm birth, as compared to an 0.68 % (95 % CI: 0.49–0.87 %) increase for exposure in the third trimester. The effect of exposure during the first trimester was not found to be statistically different from zero. The same regression models estimated with a logit model resulted in qualitatively similar results albeit with associations measured as odds ratios rather than marginal effects (Fig. S3a).

In order to examine the stability of our main estimate we also carried out a series of robustness checks (Fig. S4). First, we estimated the unadjusted version of the main model that included the same zip-code by month and county by year dummies but omitted the mother and child covariates. Next, we limited the sample to first births to account for the increased likelihood of a second preterm birth, conditional on a first. We estimated the model limited to Hispanic mothers because they are the least likely to smoke, and we included self-reported covariates indicating a dummy for whether a mother self-reported smoking cigarettes during pregnancy. Lastly we included mean temperature during pregnancy. Each of these models produced results that were statistically indistinguishable from the results in our main model.

Effects of smoke by $PM_{2.5}$ intensity were also estimated across the entire pregnancy and by trimester (Fig. 3b). In all cases the effect of an additional low-intensity smoke-day (plume overhead but smoke $PM_{2.5} < 5 \mu g/m^3$) were not statistically different from zero. Across the entire pregnancy period associated risks were similar for exposure to smoke-days of medium and high intensity. Exposure to an additional medium intensity smoke-day ($PM_{2.5} 5\text{--}10 \mu g/m^3$) was associated with an 0.95 % (95 % CI: 0.47–1.42 %) increase in the risk of preterm birth and exposure to a high intensity smoke-day ($PM_{2.5} > 10 \mu g/m^3$) was associated with an 0.82 % (95 % CI: 0.41–1.24 %) increase in risk. While the estimated association with medium intensity smoke-days was slightly higher than for high intensity smoke-days, these estimates were not statistically different from each other. However, for both medium and high intensity smoke-days, estimated associations were nearly twice as large as they were for the model that included smoke-days of all types.

Results by trimester exhibited similar patterns with no association detected for any trimester for low intensity smoke-days and effects of medium and high intensity smoke-days in the second and third trimester substantially larger than the respective association estimated for all types of smoke-days. These associations were also estimated with a logit model and presented in the supplement as odds ratios (Fig. S3b).

Heterogeneous Effects - We performed a heterogeneity analysis for sub-groups by zip-code income, mother's race/ethnicity, and baseline zip-code smoke exposure. The burden of wildfire health impacts depends both on patterns of exposures (discussed above) and, for a given level of exposure, marginal impacts per unit of exposure for different sub-groups (discussed here).

We estimated the effect of one additional smoke day for each sub-group, looking at differences in both absolute impacts (changes in rates) and relative impacts (percentage change above group-specific baseline rate). The marginal impact of an additional smoke day during the pregnancy was similar across income and race/ethnic groups in relative terms (Fig. 4 top and middle panels), and we found no statistically significant differences among either income or racial/ethnic sub-groups, although our point estimate for Black mothers was at least a third higher than for other racial or ethnic groups in absolute terms, consistent with existing evidence that Black women have persistently higher rates of preterm birth due to various factors such as institutional racism that increase vulnerability to environmental and other stressors (Mendez et al., 2014; Dominguez, 2008; Gee and Payne-Sturges, 2004).

The only sub-group analysis where we found consistent and substantial differences across groups for both relative and absolute outcomes was the split by baseline average smoke exposure. Children born to mothers residing in zip codes with higher baseline average smoke were found to be less effected by an additional day of wildfire smoke than children born to mother's residing in zip codes with infrequent smoke exposure ($p < 0.01$). Similar patterns were found when comparing any of the higher than average smoke exposure groups to the lowest smoke exposure group (Fig. 4 bottom panel). Effects were three times larger for children born to mothers in locations with the most infrequent smoke exposure as compared to children born to mothers in locations with the most frequent smoke exposure.

PTB Severity - As a secondary analysis, we estimated the effect of wildfire smoke exposure on more severe preterm births and found effects to be larger in percentage terms but less precisely estimated (Fig. S5). We estimated that an additional smoke day during pregnancy was associated with an 0.88 % (95 % CI: 0.52–1.24 %) increase in the risk of PTB < 32 weeks and an 0.55 % (95 % CI: 0.051.15 %) increase in

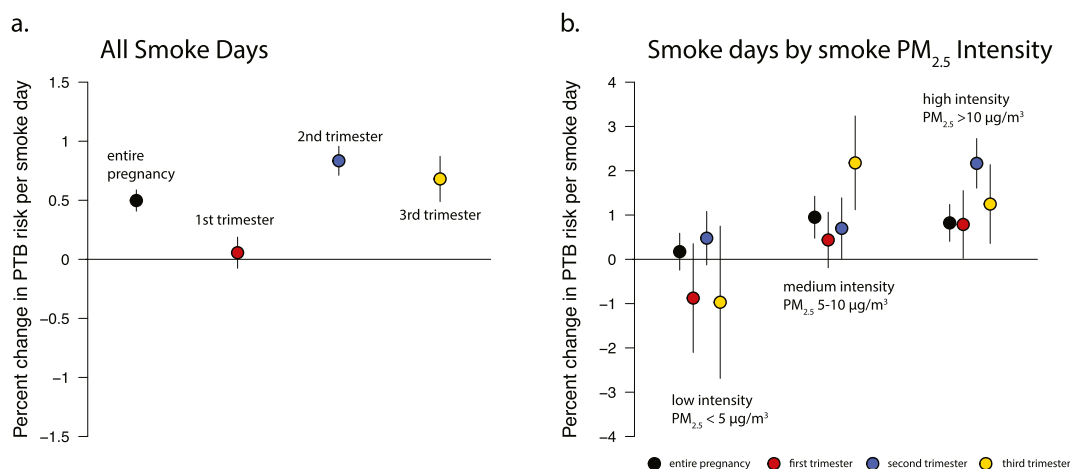


Fig. 3. Associations between smoke exposure and risk of preterm birth (< 37 weeks). Associations between preterm birth and smoke exposure across the pregnancy and by trimester estimated by separate regressions. Panel a shows estimated associations for any type of smoke-day. Panel b shows estimated associations for low, medium, and high intensity smoke-days where intensity is determined by the size of the $PM_{2.5}$ anomaly on the smoke-day. Note the scales of the y-axes differ across panels.

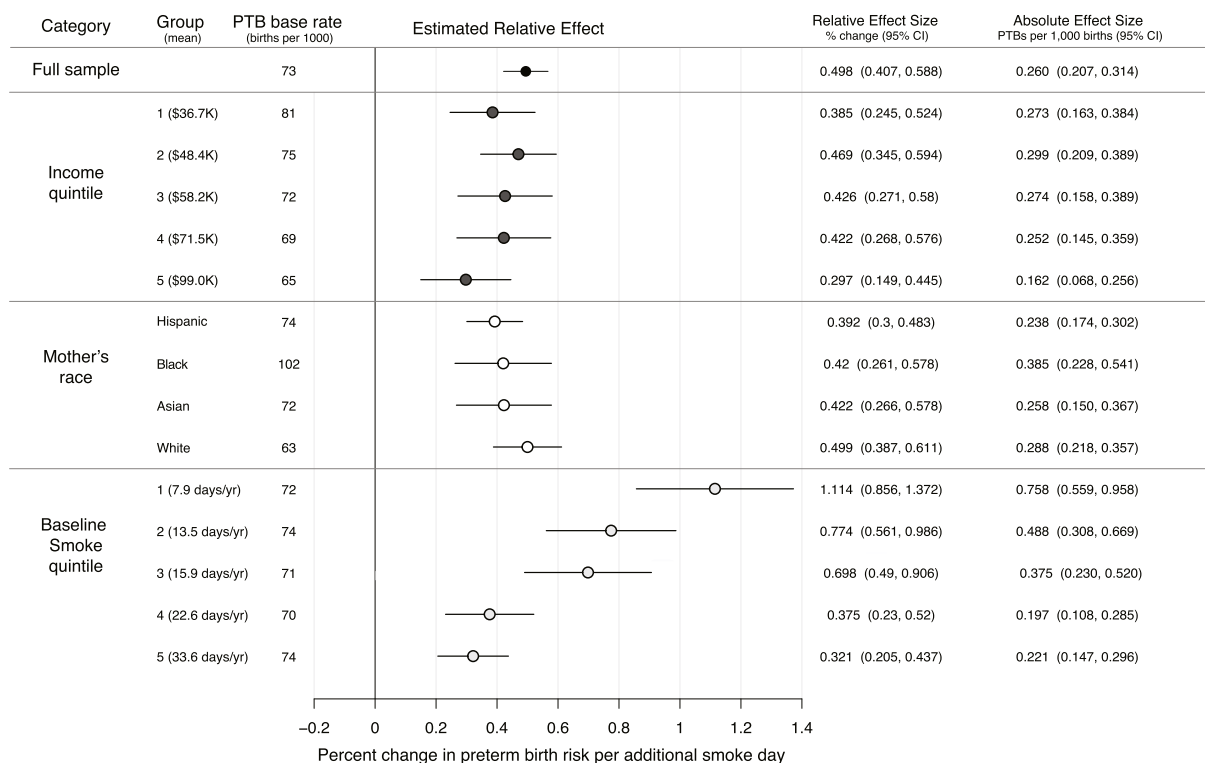


Fig. 4. Estimated effects of smoke exposure on preterm birth (< 37 week) by sub-group. The first row shows the full sample (Equation (1)) and subsequent rows show effect estimates for different sub-groups (Equation (2)).

the risk of PTB < 28 weeks. For both of the more severe preterm birth types, second trimester exposure was found to matter more than first trimester exposure. Third trimester exposure was not estimated because a substantial portion of the severe preterm births occurred prior to the start of the third trimester.

PTB Subtype - In order to better understand potential pathways, we estimated our main models separately for spontaneous and medically indicated PTBs. In total, we observed 159,950 spontaneous PTBs and 47,159 medically indicated PTBs in our sample. We did not find

meaningful differences across PTB subtypes with either model for full-pregnancy exposure or exposure by trimester. For both PTB types and with both models we found results similar to our main analysis: the second and third trimesters were the important exposure periods. Effects for medically indicated PTBs were slightly larger than for spontaneous PTBs in the third trimester and slightly smaller in the second trimester but these estimates were not statistically distinguishable from each other and, in the case of third trimester exposure, were not statistically different from zero. In summary we did not find evidence of differences

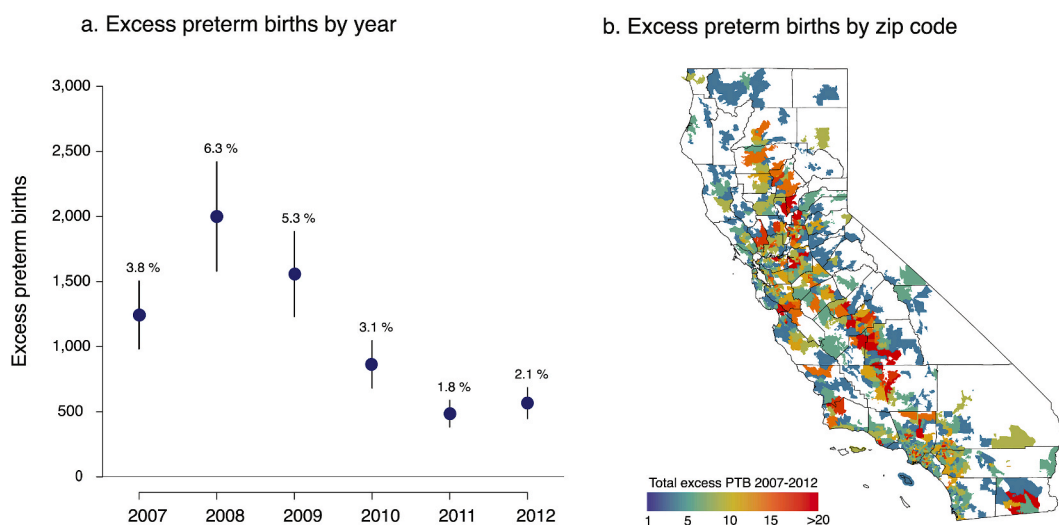


Fig. 5. Model predicted 37 week preterm births attributable to wildfire smoke exposure. Our model predicted 6,974 (95 % CI: 5,513–8,437) preterm births attributable to wildfire smoke exposure across the years 2007–2012. This accounted for 3.7 % (95 % CI: 2.9–4.5 %) of the 187,913 observed preterm births. a. Annual number of preterm births attributable to wildfire smoke exposure predicted by our model. Percentages shown above estimates indicate the estimated share of observed preterm births attributable to wildfire smoke in that year. b. Zip code level total model predicted preterm births from 2007 to 2012. White indicates there were no predicted preterm births from smoke either because smoke exposure was low or because there were a small number of observed births in that zip code.

by PTB subtype in this setting.

Attribution Estimates - Our model predicted 6,974 (95 % CI: 5,513–8,437) preterm births attributable to wildfire smoke exposure across the years 2007–2012 (Fig. 5). This accounted for 3.7 % (95 % CI: 2.9–4.5 %) of the 187,913 observed preterm births during this period. Annual percentages of preterm births attributable to smoke ranged from as low as 1.8 % in 2011 (a low smoke year) to as high as 6.3 % in 2008 (a high smoke year).

4. Discussion

We used statistical methods with satellite derived smoke plumes to estimate the effect of wildfire smoke exposure during pregnancy on preterm birth in California. We found a statistically significant relationship between smoke exposure and risk of pre-term birth, with each additional smoke day increasing the risk of preterm birth for all evaluated preterm birth severities. Consistent with previous literature focusing on wildfire smoke exposure during pregnancy (Holstius et al., 2012; Abdo et al., 2019), associations were found later in the pregnancy with the largest effects in the second trimester. This pattern was apparent both when we estimated effects of any smoke exposure and when we estimated the effect of smoke exposure separately by PM_{2.5} intensity. This differs somewhat from findings in studies examining all source PM_{2.5} exposure where the third trimester has been identified as the most important exposure period (Klepac et al., 2018; Stieb et al., 2012; Morello-Frosch et al., 2010). Potential explanations for this discrepancy include differences in exposure patterns, differences in composition between wildfire smoke and other sources of PM_{2.5}, and imprecision in identifying the start and end of trimesters.

Across exposure periods we observed a clear difference between exposure to low intensity and exposure to medium or high intensity smoke-days. However, the estimated associations for medium and high intensity smoke-days as they were defined were not statistically different from each other. Collectively these results indicate that associations between wildfire smoke and preterm birth are likely driven by exposures on the less frequent but higher intensity smoke-days.

Our heterogeneity analysis indicated the burden of exposures to wildfire smoke differed from the burden of exposure to total PM_{2.5} both across racial/ethnic groups and incomes. White mothers residing in zip-codes in the bottom 40 percentile of income were exposed most frequently to smoke, while total PM_{2.5} (from all sources) disproportionately affected low income minority communities (Fig. S2) consistent with previous studies (Jones et al., 2014; Miranda et al., 2011). In contrast to the patterns of exposure, we did not find differences in the relative effect of an additional smoke day across income or race/ethnicity (Fig. 4). Taken together, our findings on the patterns and impacts of smoke exposure thus differed somewhat from the standard narrative in the environmental justice literature, which finds strong income and racial gradients in exposure and impacts of various environmental pollutants. We found that smoke exposure had fairly consistent negative impacts on pre-term birth across population subgroups.

The estimated impact of an additional day of smoke exposure depended strongly on baseline average smoke exposure, with mothers residing in zip codes with frequent smoke exposure much less sensitive to one additional day of wildfire smoke than mothers in locations with infrequent smoke exposure. The finding of larger health impacts for less-frequently-exposed groups is consistent with findings in a recent study of wildfire smoke impacts on the Medicare population (Miller et al., 2019) and with findings on the broader effects of PM_{2.5} on mortality in the US. (Deryugina et al., 2020) There are at least four possible explanations why less-frequently-exposed mothers could be more vulnerable to wildfire smoke. First, mothers in high exposure areas could be adapting to repeated exposure (e.g. by taking effective preventative measures). Second, the effect of additional smoke on preterm birth could be non-linear, flattening out at higher levels. Third, perhaps mothers who are most sensitive to smoke exposure avoid areas that are more smoke

exposed on average (e.g. choosing to live in areas with less frequent smoke). Finally, some other moderator could co-vary with average smoke exposure – although we note that this moderator would have to be uncorrelated with income or race/ethnicity, as these latter variables do not appear to be moderators. Distinguishing the importance of these different explanations will be empirically challenging, and will likely require more detailed data on household's avoidance behavior and underlying susceptibility than our data can currently provide.

We estimated that 3.7 % of preterm births in our sample were attributable to wildfire smoke exposure. These results are broadly consistent with a recent study (Trasande et al., 2016) which estimated that, on average, nearly 5 % of all preterm births in California were attributable to total PM_{2.5}, and new evidence that wildfire smoke accounts for more than half of PM_{2.5} exposure in high smoke years in California (Burke et al., 2021).

There are a number of strengths to our study. Our sample included three million births and covered a wide range of exposures and socio-economic groups. The large sample with repeated observations in the same zip codes allowed us to use statistical methods capable of isolating variation in wildfires smoke exposure plausibly uncorrelated with the many other time-invariant and time-varying factors that affect risk of preterm birth. In addition, we were able to test for statistical differences in impacts across exposures and socioeconomic groups. Our finding that income was not protective of these effects has important implications for targeting effective mitigation or protection policies. In addition, we were able to provide evidence on the relative importance of timing and intensity in the association between wildfire smoke exposure and preterm birth.

A potential weakness of our study is possible imprecision in our measurement of smoke exposure. We assigned exposure based on mother's zip code of residence but smoke exposure could possibly vary within zip codes. In addition, we did not observe where women work, and instead our exposure measure was limited to place of residence which could lead to mismeasurement for women who spend substantial time outside of the residence zip code. The satellite-derived smoke plumes utilized in the analysis are also imperfect measurements of smoke exposure in several ways. Cloud cover can prevent identification of smoke leading to underestimation of the number or extent of smoke plumes on cloudy days. We did not observe the height of smoke plumes in the column likely leading to overestimation of the number of days when smoke was near enough to ground level to affect local pollution. The plume measures also did not include information on smoke intensity. We used local surface PM_{2.5} anomalies to characterize smoke intensity on smoke-days. However, this approach relied on the plume boundaries to attribute PM_{2.5} anomalies to smoke and thus were subject to the same limitations of mischaracterized plume boundaries. In addition, there is uncertainty associated with the PM_{2.5} estimates, particularly when smoke is present (Reid et al., 2021), which could lead to mis-assignment of smoke intensity. Our approach to assigning intensity also assumed PM_{2.5} concentrations were representative of smoke intensity whereas other pollutants in smoke, which may or may not co-vary with PM_{2.5}, could also affect risk of preterm birth. Imprecision in the timing of exposure due to uncertainty around conception date may have also lead to imprecise exposure measurements. If these errors in exposure are classical, then our estimated effects of smoke exposure on preterm birth will be attenuated toward zero. Similarly, while we estimated separate effects by trimester, if critical exposure windows do not align with trimesters then our exposure measure would not fully capture the consequences of exposure (Wilson et al., 2017). Lastly, our sub-group analysis relied on interacting smoke exposure with socio-economic and demographic features which may be correlated with additional unmeasured moderators.

To our knowledge only one previous study has examined the effect of wildfire smoke exposure during pregnancy on preterm birth (Abdo et al., 2019). That study used similar data with different methods for both characterizing exposure and estimating impacts, and was carried out on

a sample with substantially lower background pollution and smaller changes in PM_{2.5} from smoke exposure than we observed. While the units are not directly comparable between studies (smoke-days versus average $\mu\text{g}/\text{m}^3$ of PM_{2.5} from smoke), our estimated effects on 37 week preterm birth from smoke exposure across pregnancy and later in the pregnancy were qualitatively consistent with these earlier results.

PM_{2.5} is the pollutant in wildfire smoke most directly associated with harmful health impacts including preterm birth. However, there are a number of potential reasons why an increase in PM_{2.5} driven by wildfire smoke could have different impact than an increase in PM_{2.5} driven by other sources. First, wildfire smoke exposure tends to occur in short intense periods, often one to 2 weeks at a time. This structure of exposure makes avoidance more straightforward because it requires limiting ambient exposures during a short but intense period in which air quality issues might be salient, rather than sustained behavioral changes due to gradual rises in PM_{2.5} which may be less obviously detected. Second, the components of PM_{2.5} emitted from wildfires may differ in ways that matter for health. Obtaining more comprehensive speciated measures of smoke-derived PM_{2.5} (and associated other pollutants) is a critical area for future research.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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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.2021.111872>. Code used in this study can be found online at <https://github.com/sheftneal/EnvRes2021>.

Contributions

SHN, GS, and MB conceived of the paper. SHN, AD, and WY processed data. SHN, AD, and MB analyzed data. All authors contributed to interpreting the results and writing the paper.

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