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## Pregnancy Exposure to PM<sub>2.5</sub> from Wildland Fire Smoke and Preterm Birth in California

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### Summary

**Background**—Wildfires in the Western United States are a growing and significant source of air pollution that is eroding decades of progress in air pollution reduction. The effects on preterm birth during critical periods of pregnancy are unknown.

**Methods**—We assessed associations between prenatal exposure to wildland fire smoke and risk of preterm birth (gestational age <37 weeks). We assigned smoke exposure to geocoded residence at birth for all live singleton births in California conceived 2007–2018, using weekly average concentrations of particulate matter 2.5 microns (PM<sub>2.5</sub>) attributable to wildland fires from United States Environmental Protection Agency’s Community Multiscale Air Quality Model. Logistic regression yielded odds ratio (OR) for preterm birth in relation to increases in average exposure across the whole pregnancy, each trimester, and each week of pregnancy. Models adjusted for season, age, education, race/ethnicity, medical insurance, and smoking of the birthing parent.

**Results**—For the 5,155,026 births, higher wildland fire PM<sub>2.5</sub> exposure averaged across pregnancy, or any trimester, was associated with higher odds of preterm birth. The OR for an increase of 1µg/m<sup>3</sup> of average wildland fire PM<sub>2.5</sub> during pregnancy was 1.013 (95% CI:1.008,1.017). Wildland fire PM<sub>2.5</sub> during most weeks of pregnancy was associated with higher odds. Strongest estimates were observed in weeks in the second and third trimesters. A 10µg/m<sup>3</sup>

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Author Contributions

SP performed statistical analyses and drafted manuscript; SH, FL, NP, SYC, and AM estimated wildland PM<sub>2.5</sub> exposures; DEG and RS provided significant editing; EN, RMF, FL, SH and AMP obtained funding; AMP conceived of the project; all authors reviewed and edited the drafted manuscript.

Competing Interests

The authors declare no competing interests.

increase in average wildland fire PM<sub>2.5</sub> in gestational week 23 was associated with OR=1.034; 95% CI: 1.019, 1.049 for preterm birth.

**Conclusions**—Preterm birth is sensitive to wildland fire PM<sub>2.5</sub>; therefore, we must reduce exposure during pregnancy.

### Keywords

air pollution; pregnancy; preterm birth; wildfire; fire; PM<sub>2.5</sub>

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## Introduction

Wildfires are a significant source of air pollution in the Western United States (US),<sup>1</sup> eroding the progress made in reducing air pollution over several decades.<sup>2,3</sup> Effects of wildfire smoke on preterm birth are not well understood.<sup>4–7</sup> Preterm birth (birth at less than 37 weeks gestation) affects approximately 8% of singleton births in the US<sup>8</sup> and is an important risk factor for perinatal mortality and morbidity in childhood and adulthood, including pulmonary and neurodevelopmental outcomes.<sup>9</sup>

Prior studies have shown that preterm birth risk is sensitive to prenatal exposures to ambient air pollution, including fine particulate matter <2.5 microns (PM<sub>2.5</sub>) and polycyclic aromatic hydrocarbons, a by-product of combustion, in California.<sup>10–13</sup> Furthermore, studies have demonstrated that exposures to high levels of PM<sub>2.5</sub> in the second trimester and near the end of pregnancy are most critical with regard to risk of preterm birth,<sup>10,14</sup> and that associations are stronger for earlier (*i.e.*, more severe) preterm births.<sup>10</sup> It was estimated that between 2.7–3.4 million preterm births were associated with PM<sub>2.5</sub> exposure globally in 2010.<sup>15</sup>

Several studies around the globe have examined wildfire smoke during pregnancy and risk of preterm birth, though with varying exposure assessment approaches, statistical methods and results.<sup>5–7,16</sup> To date, previous studies used ZIP code level or larger geographic areas to assign smoke exposure and have been limited to trimester specific exposures to assess potentially critical exposure windows during pregnancy. Most previous studies found positive associations between prenatal wildfire smoke exposure and preterm birth, particularly in the second trimester.

The intensity and duration of air pollution exposures during recent California wildfire events are beyond the exposure ranges generally examined in previous studies,<sup>17</sup> resulting in a gap in knowledge on the perinatal health effects of wildfires. We examine weekly prenatal exposure to wildland fire-related PM<sub>2.5</sub> estimated at the geocoded residence of the parent giving birth in relation to risk of preterm birth in California in the largest investigation to date.

## Materials and Methods

### Study Population

The cohort consists of all live singleton births in California conceived between January 1<sup>st</sup>, 2007 and December 31<sup>st</sup>, 2018, including births that occurred in 2019, as determined by

date of birth and gestational age in weeks and days. Birth certificate data were provided by the California Department of Public Health and included information on the race/ethnicity, education, smoking status, residential address, and age of the parent giving birth, and expected payer for delivery costs (*i.e.*, insurance type). We geocoded the residential address of the parent giving birth to a latitude and longitude using ArcGIS (Esri, Redlands, California). Births from 2007–2019 were excluded if conceived in 2006 or 2019 (~8%); if the residential address could not be geocoded (~5%); if gestational age was reported as less than 20 weeks, greater than 44 weeks, or missing (<1%); if exposure data were not available (<1%); if the age of the parent giving birth was under 13 years, over 55 years, or missing; or if information on delivery insurance, smoking, or education of the parent giving birth was missing (Figure S1). Births excluded due to missing covariates (other than exposure and gestational age) were approximately 5% of the total.

The study was approved by the University of California, Berkeley (#2013-10-5693), University of California, San Francisco (#19–28443), and the California Health and Human Services Agency (#13-05-1231) committees for the protection of human subjects.

### Exposure Assessment

The US Environmental Protection Agency (EPA) provided ambient PM<sub>2.5</sub> daily concentrations with and without wildland fire emissions that were simulated using the Community Multi-scale Air Quality model (CMAQ).<sup>18</sup> CMAQ is a three-dimensional Eulerian chemical transport model (CTM) that simulates atmospheric transport and dispersion of VOC, NO<sub>x</sub>, CO, SO<sub>2</sub>, and PM emissions as well as the atmospheric chemistry and deposition of gases and aerosols. This CTM was selected because of its detailed representation of atmospheric processes and ability to simulate the contribution of wildland fire emissions in the context of emissions from other natural and anthropogenic sources.

The model was applied to the continental US with 12 km resolution for 2007–2018. Our focus is on exposures in California; however, by applying the model for a larger domain, the simulated concentrations include contributions of emissions from California and surrounding states. A detailed description of the methodology and model performance is provided by Koman *et al.*<sup>19,20</sup>

The raw CMAQ estimates tend to underestimate the observed PM<sub>2.5</sub> levels and have significant error. We implemented bias-correction to improve the spatial-temporal accuracy of the exposure assignments by fusing the 12 km CMAQ model daily estimates with EPA Air Quality System (AQS) ambient air quality observations using the three-step method of Friberg *et al.*<sup>21</sup> The details of the method are described in the Supplement. To summarize, the first step involves ordinary Kriging of the observations, with the annual mean CMAQ field providing spatial structure throughout the domain. A second step involves scaling daily CMAQ simulated fields using mean observations to reduce bias. Finally, a weighted average of these results based on prediction of temporal variance provides optimized daily estimates for each 12 km grid. The bias-correction was performed using daily data; however, the model performance relevant for this epidemiologic study is the weekly performance. The bias, error, and coefficient of determination (R<sup>2</sup>) for the weekly PM<sub>2.5</sub> exposure concentrations determined by leave-one-out cross-validation are listed (Table 1). The data

fusion not only reduces the mean bias to less than  $0.6 \mu\text{g}/\text{m}^3$ , but also decreases the mean error in weekly  $\text{PM}_{2.5}$  from 4.3 to  $2.9 \mu\text{g}/\text{m}^3$ , decreases the mean fractional bias from  $-17\%$  to  $-7\%$ , decreases the mean fractional error from 45% to 31%, and increases  $R^2$  from 0.27 to 0.55 for the overall period. Scatter plots of the raw and bias-corrected predicted and observed weekly  $\text{PM}_{2.5}$  concentrations (Figure S3) and time-series plots (Figure S5) illustrate performance during the 2008 high fire year at representative monitoring locations.

Under most circumstances, CTM model adjustments that are based on total  $\text{PM}_{2.5}$  mass would apply to all PM chemical constituents and source contributions in proportion to  $\text{PM}_{2.5}$  mass. However, for CTM simulations involving large wildland fires, additional consideration is given to circumstances where the bias-correction produced increased concentrations that far exceeds concentrations expected from conventional non-wildfire sources. Using the bias-corrected CMAQ estimates, we computed the 95<sup>th</sup> percentile daily  $\text{PM}_{2.5}$  concentration on days when the NOAA HMS indicated no smoke in each grid. We capped adjustments in non-fire  $\text{PM}_{2.5}$  at this historical 95<sup>th</sup> percentile of concentrations in case where bias corrections increased concentration  $>5\mu\text{g}/\text{m}^3$  and assume the remainder of the adjustment applies to the wildland fire  $\text{PM}_{2.5}$ . Details of the adjustment procedure are described in the Supplement.

Daily average  $\text{PM}_{2.5}$  concentrations with and without wildland fire emissions were extracted from bias-corrected CMAQ runs for the grid for each birth residence over the pregnancy period and aggregated to assign average weekly exposures during pregnancy. These values were used to calculate the incremental impact from the wildland fire emissions, which is defined as the difference of the with fire scenario and the without wildland fire scenario. For the analyses presented here, the exposures are these wildland fire increments, representing the estimated average  $\text{PM}_{2.5}$  concentrations due to wildland fire smoke in each week (or trimester) of pregnancy, truncated to 37 weeks for analyses of preterm birth and to 32 weeks for analyses of early preterm birth. The area burned by prescribed fires was low relative to wildfire area burned in California (less than 3% most years), therefore, in this analysis, it is assumed that the CMAQ wildland fire smoke is representative of wildfire smoke even though it contains a small amount of smoke from prescribed burns (Figure 1).

Some pregnancies conceived in 2018 ended in 2019; however, CMAQ exposures were not available in 2019, which was a year with considerably fewer and smaller fires in California (*i.e.*, 259,823 acres in 2019 compared to 1,975,086 acres in 2018<sup>22</sup>). Each pregnancy contributed to analyses for all weeks (and trimesters) that occurred fully within the period 2007–2018. This resulted in different numbers of pregnancies contributing to the analysis for each week, as births occurring in 2019 only contributed exposure data during gestational weeks that occurred in 2018.

## Outcome Assessment

Gestational age was assigned based on the best obstetrical estimate (combination of date of last menstrual period and ultrasound). Preterm birth was defined as birth  $<37$  weeks gestation. Early preterm birth was defined as delivery at  $<32$  weeks gestation.

## Statistical Analysis

We first examined whether risk of preterm birth was elevated with higher average exposure to wildland fire PM<sub>2.5</sub>, both for exposures over the whole pregnancy and during each trimester. For these analyses we ran logistic models using the average exposure over the corresponding period of the pregnancy (truncated to the appropriate endpoint of 37 or 32 weeks for the two outcomes) and considered an increase of 1µg/m<sup>3</sup> concentration of wildland fire PM<sub>2.5</sub>.

However, averaging exposure over an entire pregnancy or trimester dilutes the intensity of exposure; exposures are potentially diluted more for longer pregnancies. Given that wildfire smoke is not a persistent exposure following similar daily patterns over the entire pregnancy period but rather an intermittent exposure that could be quite high for a week or more but low for the rest of the pregnancy, analyses focusing on the exposure in each week of pregnancy have the advantage of capturing the full range of intermittent exposures experienced while comparing their potential impacts on pregnancies that are at the same stage of gestation.

To assess whether wildland fire PM<sub>2.5</sub> exposures during certain weeks of pregnancy may be critical with respect to preterm birth risk, we ran separate logistic regressions of wildland fire PM<sub>2.5</sub> exposure experienced in each week of pregnancy on preterm birth occurring at any time thereafter. There were 37 separate logistic regression analyses considering preterm birth as the outcome, one for each pregnancy week at risk, and 32 separate analyses considering early preterm birth as the outcome. Exposure in each week was treated as linear, and we considered an increase of 10µg/m<sup>3</sup> concentration of wildland fire PM<sub>2.5</sub> because the range of exposures for a single week of the pregnancy was greater than the range of exposures when averaged over the entire pregnancy or a trimester. In case of nonlinear effects, we also ran a set of analyses comparing the highest quartile of exposure to the lowest.

All models adjusted for the following potential confounders: season of conception (two continuous functions: sine and cosine of  $2\pi$  times the elapsed fraction of the year on the date of conception), health insurance type (indicator for delivery costs paid by Medi-Cal [public health insurance] vs private or other insurance) and the following characteristics of the parent giving birth: age (<20, 20–35, >35 years), education level (category indicators for less than high school, high school diploma, some college, college degree or more), race/ethnicity indicators (non-Hispanic white, non-Hispanic Black, non-Hispanic Asian-American/Pacific Islander, missing/non-Hispanic other, Hispanic), and smoking status (self-report of ever/never smoked). In our study population, education and medical insurance were considered markers of socioeconomic status, and race/ethnicity was included as a proxy for having experienced structural and/or interpersonal racism, a known risk factor for preterm birth.<sup>23</sup>

We performed several sensitivity analyses to test the robustness of our findings. To check for spatial confounding, we adjusted for county of residence. To address potential trends, we adjusted for year of conception. We additionally adjusted for non-fire-related PM<sub>2.5</sub> exposure. We performed an analysis including imputed exposure data in 2019 (using a different data source as described in the Supplement), including all pregnancies conceived

2007–2018. This analysis avoided fixed cohort bias potentially caused by over-selecting shorter pregnancies at the end of the cohort.<sup>24</sup>

## Results

As indicated above, fusion of the raw CMAQ estimates with ambient observations improved the accuracy of the weekly PM<sub>2.5</sub> values used for exposure assignment. The pregnancy average total PM<sub>2.5</sub> and wildland fire PM<sub>2.5</sub> exposure were 10.2 and 0.9 µg/m<sup>3</sup> (Table 2). The pregnancy average wildland fire PM<sub>2.5</sub> ranged from 0.2 to 1.9 µg/m<sup>3</sup> and 3% to 18% of total PM<sub>2.5</sub> in different years. The wildland fire estimates at the residences are lower than the grid average exposures (~ 2 µg/m<sup>3</sup>) on average.

The estimated spatial distribution of wildland fire PM<sub>2.5</sub> exposure in the 2007–2018 period (Figure 2) indicates higher exposures in northern and central California than southern California, and higher exposure in the Coastal Range and Sierra Nevada Mountains than in the major metropolitan areas. The populated regions of California have long-term wildland fire PM<sub>2.5</sub> in the 0.5 to 1.5 µg/m<sup>3</sup> range; however, during weeks of highest fire activity during the study period (e.g., those shown in Figures 3–4), the estimated wildland fire PM<sub>2.5</sub> concentrations exceeded 100 µg/m<sup>3</sup> near major wildfires. Areas with highest estimated weekly wildland fire PM<sub>2.5</sub> exposure were in 2008 in the Northern California Coastal and Sierra Nevada mountains, coastal California southwest of Big Sur, and eastern Kern County (Figures 3). In 2018, the Northern California Coastal mountains, Sierra Nevada Mountains near Mt Lassen, south of Lake Tahoe and West of Yosemite National Park were high wildland fire PM<sub>2.5</sub> areas (Figure 4). During weeks with high fire activity, smoke is transported to California's Central Valley, and major metropolitan areas of Sacramento, San Francisco, and Los Angeles. Overall, estimates suggest residents in every part of California were exposed to measurable amounts of wildland fire PM<sub>2.5</sub>.

California recorded 5,665,097 resident live births with conception dates from 2007 through 2018 and parental residence at birth that could be geocoded. The final analysis dataset contained 5,155,026 singleton births (Table 3). Preterm birth was more likely if the parent giving birth was <20 or ≥35 years of age, had lower educational attainment, was Black, Asian/Pacific Islander, Hispanic, or had missing/other race/ethnicity, had Medi-Cal insurance, or ever smoked cigarettes (Table 2). Preterm birth risk was also higher for pregnancies conceived in spring (March–May).

Higher wildland fire PM<sub>2.5</sub> exposure overall or during any trimester was associated with higher risk of preterm or early preterm birth, though for early preterm birth the association was not significant for exposure averaged over the whole pregnancy or the first trimester. An increase of 1 µg/m<sup>3</sup> in the average exposure to wildland fire PM<sub>2.5</sub> across the whole pregnancy was associated with elevated odds of preterm birth (OR=1.013, 95% CI 1.008–1.017). The corresponding ORs of preterm birth for the same increase in exposure during trimester 1 was 1.007 (1.004–1.010), and during trimesters 2 and 3, the ORs were 1.008 (1.005–1.011) and 1.010 (1.007–1.012), respectively. For early preterm birth, the estimates were 1.004 (0.993–1.015) for exposures across the whole pregnancy, and 1.004 (0.996–



1.011), 1.007 (1.000–1.015), and 1.007 (1.001–1.012) for exposures during trimesters 1–3, respectively.

In analyses of exposure by week of pregnancy, wildland fire PM<sub>2.5</sub> in nearly any week was associated with increased risk of preterm birth (Figure 5; Table S2). There was no clear evidence for a specific window of vulnerability, though the strongest estimates were observed in weeks in the second and third trimesters. For example, a 10µg/m<sup>3</sup> increase in wildland fire PM<sub>2.5</sub> in week 23 of pregnancy was associated with a higher risk of preterm birth (OR=1.034; 95% CI: 1.019, 1.049). Results from analyses comparing the highest quartile to the lowest quartile of exposure in each week showed a similar pattern to those observed in the main analyses, except in weeks 35–37 when they were lower; the odds ratio in week 23 was 1.025 (95% CI: 1.014, 1.036). Estimates from sensitivity analyses are presented in Supplemental Material (Figure S4). Results did not notably change when models were additionally adjusted for cumulative non-fire PM<sub>2.5</sub> exposure or county, or when imputed exposures for pregnancy weeks occurring in 2019 were included; they were somewhat lower when adjusted for year of conception.

Increased risk of early preterm birth was observed for wildland fire PM<sub>2.5</sub> exposure for only certain weeks (*e.g.*, in week 23, OR for 10µg/m<sup>3</sup> increase in wildland fire PM<sub>2.5</sub> =1.066; 95% CI: 1.031, 1.103), and estimates were closer to the null when comparing the highest to the lowest exposure quartile (Figure 6; Table S3). The pattern of estimates over time was similar in all sensitivity analyses, with adjustment for year of conception slightly attenuating the estimates (Figure S5).

## Discussion

These analyses suggest that exposure at any point during pregnancy is likely to increase risk of preterm birth, but we did not find evidence for any particular exposure window during pregnancy that is more vulnerable to exposure to wildland fire PM<sub>2.5</sub>. This finding is consistent with previous studies that have found increased risk of preterm birth associated with wildland fire smoke exposure;<sup>5–7,16</sup> however, this study is the largest to date, includes more recent fires that occurred in California, and is the first to examine exposure for each week of pregnancy and undertake spatially resolved exposure assignment at the geocoded residence of the parent giving birth. Another important strength of this study is that we avoided fixed cohort bias by using conception dates rather than birth dates to define our cohort.

Four previous studies have found associations between wildland fire smoke exposure during pregnancy and risk of preterm birth in Colorado,<sup>7</sup> California,<sup>5</sup> Brazil,<sup>6</sup> and Australia.<sup>16</sup> In a study of 535,895 pregnancies in Colorado between 2007–2015, Abdo *et al.* examined PM<sub>2.5</sub> concentrations from wildland fire smoke at the ZIP code level during each trimester and found that a 1µg/m<sup>3</sup> increase in second trimester exposure was associated with 13% increased risk of preterm birth.<sup>7</sup> In California, approximately 3 million pregnancies between 2006–2012 were used to estimate risk of preterm birth in relation to smoke exposure at the ZIP code level based on satellite-based estimates of wildland fire smoke plume boundaries and gridded estimates of surface PM<sub>2.5</sub> concentrations.<sup>5</sup> This study found each day of



exposure to any wildland fire smoke was associated with a 0.49% (95% CI: 0.41, 0.59%) increase in risk of preterm birth. Estimates by trimester suggested stronger associations with exposure later in pregnancy and estimates were driven by higher intensity smoke days.<sup>5</sup> A case-crossover study across regions of Brazil found wildland fire exposure, as indicated by >90<sup>th</sup> percentile of ambient PM<sub>2.5</sub> and documented wildland fire occurrence, was related to preterm birth in the first trimester (OR=1.41; 95% CI: 1.31, 1.51) in the southeast and in the second trimester in the North (OR=1.05; 95% CI: 1.01, 1.09).<sup>6</sup> In New South Wales, Australia, PM<sub>2.5</sub> from wildland fire smoke was modeled to a grid resolution of 25km × 25km and assigned to maternal residence. An interquartile range increase (1.85µg/m<sup>3</sup>) in gestational exposure corresponded to higher hazard of preterm birth (HR= 1.069, 95% CI: 1.058–1.081), with strongest associations in the second trimester.

In a previous analysis, we used the generalized synthetic control method to assess critical windows of exposure to the 2018 Camp fire, one of the most damaging fires in California history. We found exposure during week 10 was consistently associated with preterm birth.<sup>25</sup> Although our estimates are modest in magnitude, they are robust to several sensitivity analyses; the analyses comparing the highest to the lowest quartile of exposure largely support our conclusion that exposure in nearly any week of pregnancy increases the risk of preterm birth. The analyses considered the impact of an increase in exposure in a single week to attempt to identify critical exposure windows, though no week was exceptionally different. We did not find higher estimates for early preterm births as we had expected based on previous findings of ambient air pollution and early preterm birth.<sup>10,11</sup> Our estimates for early preterm birth, however, may be particularly subject to survival bias, a form of left censoring owing to fetal death, as pregnancies ending before 32 weeks of gestation are more likely to end in fetal death than pregnancies ending after 32–37 weeks.<sup>26,27</sup> This could also explain why the first trimester exposures showed less of an association with early preterm birth than with preterm birth.

A limitation of our study is the uncertainty in wildland fire PM<sub>2.5</sub> exposure estimates. Despite the use of comprehensive emissions, meteorology, and chemical transport and dispersion models, the uncertainty in wildland fire PM<sub>2.5</sub> estimates is greater than for air pollution from most anthropogenic sources because emissions from wildland fires are not as easily measured or quantified as are those from smoke-stacks or tailpipes. Furthermore, the nature of the complex mixtures of particles and gases that evolve downwind are not well-characterized. Uncertainties include fire location, size, and spread rate; fuel loading and combustion efficiency; diurnal variation in emissions and plume rise; local effects of fire-induced weather that are not resolved by regional meteorological models, and the amount of secondary organic aerosol formation. Another concern is that wildland fire PM<sub>2.5</sub> estimates did not include contributions from agricultural waste and residential wood burning, which could be significant.<sup>28</sup> In addition, underestimation of total PM<sub>2.5</sub> may imply underestimation of wildland fire PM<sub>2.5</sub> on average. However, the accuracy of the CMAQ in these simulations is similar to that for other regional models in California.<sup>29,30</sup>

Exposures were assigned based on birth date and gestational age, the latter of which has some uncertainty; thus, estimates attached to specific gestational weeks should be interpreted cautiously. Another limitation is that exposure is assigned based on residential

address of the parent giving birth, which could cause exposure misclassification. It is not known whether there was a change in residence during pregnancy; however, previous studies have found these potential changes do not noticeably affect results in air pollution studies.<sup>31</sup> Time activity of our study population is not captured, and relocation, particularly if owing to wildland fire smoke exposure, would have likely altered true exposure for some individuals, perhaps those assigned the highest exposures. It is also likely that relocation and other measures to reduce exposure, such as staying indoors in well-sealed buildings with air purifiers, vary by socioeconomic status and may cause differential overestimates of exposure. Nonetheless, the quantitative estimate of PM<sub>2.5</sub> concentrations assigned to people according to their residential address is still an improvement over previous exposure assessment methods.<sup>4-7,16</sup> Finally, we acknowledge that, particularly for those living near a wildfire, psychological stress and anxiety about the fire itself (for example, if a pregnant person's home is at risk of burning down) or about its emissions could be responsible for some portion of the observed associations between wildland fire smoke and preterm birth.

Preterm birth is a heterogeneous outcome, and there is limited understanding of the mechanisms which lead to parturition.<sup>9</sup> Even less is known of the specific biological pathways by which wildland fire smoke may affect preterm birth, though multiple mechanisms could contribute. Increased inflammation, vascular and endothelial functional changes,<sup>32</sup> oxidative stress, endocrine disruption, and cellular dysfunction are potential mechanisms linking PM to preterm birth.<sup>33</sup> Additionally, DNA damage, epigenetic changes, and metabolic dysregulation may also play a role.<sup>33</sup> Furthermore, during pregnancy, respiratory rate and cardiac output are increased on average by 40% and 50%, respectively,<sup>29,30</sup> leading to increased exposure and vulnerability in the birthing parent.

In summary, exposure to wildland fire PM<sub>2.5</sub> during pregnancy was associated with increased risk of preterm birth. Further research should confirm potential critical periods of pregnancy and examine potential biological pathways by which these associations occur.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations:

<b>AQS</b>	Air Quality System
<b>CI</b>	Confidence Interval
<b>CMAQ</b>	Community Multi-Scale Air Quality
<b>CTM</b>	chemical transport model
<b>EPA</b>	Environmental Protection Agency

<b>HMS</b>	Hazard Mapping System
<b>OR</b>	Odds Ratio
<b>PM<sub>2.5</sub></b>	Particulate Matter <2.5 microns
<b>US</b>	United States

## References

- Burke M, Driscoll A, Heft-Neal S, Xue J, Burney J, Wara M. The changing risk and burden of wildfire in the United States. *Proc Natl Acad Sci USA*. 2021 Jan 12;118(2):e2011048118. [PubMed: 33431571]
- Burke M, Childs ML, De La Cuesta B, Qiu M, Li J, Gould CF, et al. The contribution of wildfire to PM<sub>2.5</sub> trends in the USA. *Nature*. 2023 Oct 26;622(7984):761–6. [PubMed: 37730996]
- Wei Y, Danesh Yazdi M, Ma T, Castro E, Liu CS, Qiu X, et al. Additive effects of 10-year exposures to PM<sub>2.5</sub> and NO<sub>2</sub> and primary cancer incidence in American older adults. *Environ Epidemiol*. 2023 Aug;7(4):e265. [PubMed: 37545804]
- Amjad S, Chojecki D, Osornio-Vargas A, Ospina MB. Wildfire exposure during pregnancy and the risk of adverse birth outcomes: A systematic review. *Environment International*. 2021 Nov;156:106644.
- Heft-Neal S, Driscoll A, Yang W, Shaw G, Burke M. Associations between wildfire smoke exposure during pregnancy and risk of preterm birth in California. *Environmental Research*. 2022 Jan;203:111872.
- Requia WJ, Papatheodorou S, Koutrakis P, Mukherjee R, Roig HL. Increased preterm birth following maternal wildfire smoke exposure in Brazil. *Int J Hyg Environ Health*. 2022 Mar;240:113901.
- Abdo M, Ward I, O'Dell K, Ford B, Pierce J, Fischer E, et al. Impact of Wildfire Smoke on Adverse Pregnancy Outcomes in Colorado, 2007–2015. *IJERPH*. 2019 Oct 2;16(19):3720. [PubMed: 31581673]
- Martin J, Osterman M. Exploring the Decline in the Singleton Preterm Birth Rate in the United States, 2019–2020 [Internet]. National Center for Health Statistics (U.S.); 2022 Jan [cited 2023 Mar 29]. Available from: <https://stacks.cdc.gov/view/cdc/112969>
- Behrman RE, Butler AS. Preterm Birth: Causes, Consequences, and Prevention. Washington D.C.; 2007. (Reports funded by National Institutes of Health, editor. The National Academies Collection).
- Padula AM, Mortimer KM, Tager IB, Hammond SK, Lurmann FW, Yang W, et al. Traffic-related air pollution and risk of preterm birth in the San Joaquin Valley of California. *Ann Epidemiol*. 2014 Dec;24(12):888–895e4. [PubMed: 25453347]
- Padula AM, Noth EM, Hammond SK, Lurmann FW, Yang W, Tager IB, et al. Exposure to airborne polycyclic aromatic hydrocarbons during pregnancy and risk of preterm birth. *Environ Res*. 2014 Nov;135:221–6. [PubMed: 25282280]
- Freije SL, Enquobahrie DA, Day DB, Loftus C, Szpiro AA, Karr CJ, et al. Prenatal exposure to polycyclic aromatic hydrocarbons and gestational age at birth. *Environment International*. 2022 Jun;164:107246.
- Klepac P, Locatelli I, Korošec S, Künzli N, Kukec A. Ambient air pollution and pregnancy outcomes: A comprehensive review and identification of environmental public health challenges. *Environ Res*. 2018 Nov;167:144–59. [PubMed: 30014896]
- Chang HH, Warren JL, Darrow LA, Reich BJ, Waller LA. Assessment of critical exposure and outcome windows in time-to-event analysis with application to air pollution and preterm birth study. *Biostatistics (Oxford, England)*. 2015 Jul;16(3):509–21. [PubMed: 25572998]
- Malley CS, Kuylensstierna JC, Vallack HW, Henze DK, Blencowe H, Ashmore MR. Preterm birth associated with maternal fine particulate matter exposure: A global, regional and national assessment. *Environ Int*. 2017 Apr;101:173–82. [PubMed: 28196630]

16. Zhang Y, Ye T, Yu P, Xu R, Chen G, Yu W, et al. Preterm birth and term low birth weight associated with wildfire-specific PM2.5: A cohort study in New South Wales, Australia during 2016–2019. *Environment International*. 2023 Apr;174:107879.
17. Aguilera R, Luo N, Basu R, Wu J, Clemesha R, Gershunov A, et al. A novel ensemble-based statistical approach to estimate daily wildfire-specific PM2.5 in California (2006–2020). *Environ Int*. 2023 Jan;171:107719.
18. Baker K Personal communication with Changsy Chang regarding the delivery of US EPA’s CMAQ output files to Sonoma Technology. 2020.
19. Koman PD, Billmire M, Baker KR, de Majo R, Anderson FJ, Hoshiko S, et al. Mapping Modeled Exposure of Wildland Fire Smoke for Human Health Studies in California. *Atmosphere*. 2019 Jun 4;10(6):308. [PubMed: 31803514]
20. Koman PD. Using wildland fire smoke modeling data in gerontological health research (California, 2007–2018). *Science of the Total Environment*. 2022;14.
21. Friberg MD, Zhai X, Holmes HA, Chang HH, Strickland MJ, Sarnat SE, et al. Method for Fusing Observational Data and Chemical Transport Model Simulations To Estimate Spatiotemporally Resolved Ambient Air Pollution. *Environ Sci Technol*. 2016 Apr 5;50(7):3695–705. [PubMed: 26923334]
22. Porter TW, Crowfoot W, Newsom G. 2018–2019 Wildfire Activity Statistics. 2019;
23. Burris HH, Lorch SA, Kirpalani H, Pursley DM, Elovitz MA, Clougherty JE. Racial disparities in preterm birth in USA: a biosensor of physical and social environmental exposures. *Arch Dis Child*. 2019 Oct;104(10):931–5. [PubMed: 30850379]
24. Strand LB, Barnett AG, Tong S. Methodological challenges when estimating the effects of season and seasonal exposures on birth outcomes. *BMC Med Res Methodol*. 2011 Dec;11(1):49. [PubMed: 21501523]
25. Goin D, Benmarhnia T, Huang S, Lurmann F, Mukherjee A, Morello-Frosch R, et al. The Camp fire and perinatal health: An example of the generalized synthetic control method to identify susceptible windows of exposure. *American Journal of Epidemiology*. in press.
26. Boutin A, Lisonkova S, Muraca GM, Razaz N, Liu S, Kramer MS, et al. Bias in comparisons of mortality among very preterm births: A cohort study. *PLoS One*. 2021;16(6):e0253931. [PubMed: 34191860]
27. Gregory E, Valenzuela C, Hoyert D. NVSR 72–8: Fetal Mortality: United States, 2021 [Internet]. National Center for Health Statistics (U.S.); 2023 Jul [cited 2024 Feb 21]. Available from: <https://stacks.cdc.gov/view/cdc/129432>
28. Noth EM, Lurmann F, Perrino C, Vaughn D, Minor HA, Hammond SK. Decrease in Ambient Polycyclic Aromatic Hydrocarbon Concentrations in California’s San Joaquin Valley 2000–2019. *Atmos Environ*. 2020 Dec 1;242:117818.
29. Hu J, Zhang H, Ying Q, Chen SH, Vandenberghe F, Kleeman MJ. Long-term particulate matter modeling for health effect studies in California – Part 1: Model performance on temporal and spatial variations. *Atmospheric Chemistry and Physics*. 2015;15(6):3445–61.
30. Simon H, Baker KR, Phillips S. Compilation and interpretation of photochemical model performance statistics published between 2006 and 2012. *Atmospheric Environment*. 2012 Dec;61:124–39.
31. Pereira G, Bracken MB, Bell ML. Particulate air pollution, fetal growth and gestational length: The influence of residential mobility in pregnancy. *Environ Res*. 2016 May;147:269–74. [PubMed: 26918840]
32. CalFire. Statistics. [Internet]. California Department of Forestry & Fire Protection, Office of the State Fire Marshal.; 2023 [cited 2023 May 30]. Available from: <https://www.fire.ca.gov/our-impact/statistics>
33. Basilio E, Chen R, Fernandez AC, Padula AM, Robinson JF, Gaw SL. Wildfire Smoke Exposure during Pregnancy: A Review of Potential Mechanisms of Placental Toxicity, Impact on Obstetric Outcomes, and Strategies to Reduce Exposure. *Int J Environ Res Public Health*. 2022 Oct 22;19(21):13727.
34. Bobrowski RA. Pulmonary physiology in pregnancy. *Clin Obstet Gynecol*. 2010 Jun;53(2):285–300. [PubMed: 20436304]

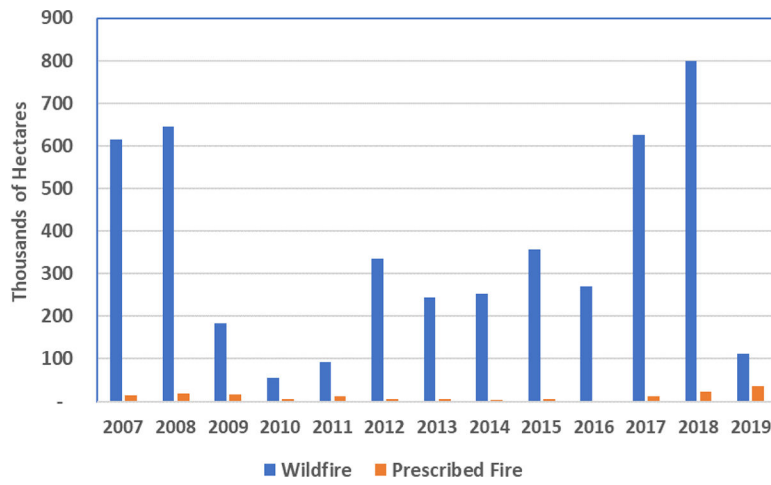
35. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol.* 2013 Dec;27(6):791–802. [PubMed: 24012425]

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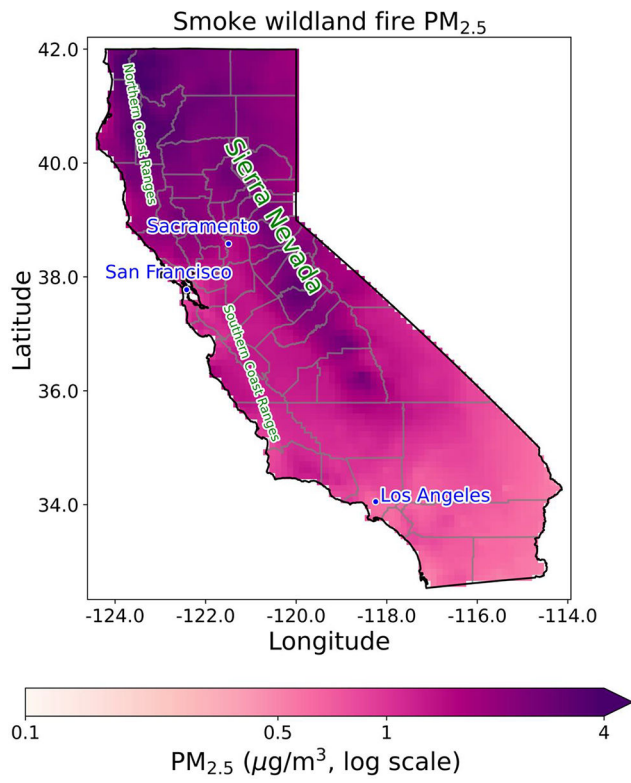
**Figure 1.** Annual size of wildfires and prescribed fires in California 2007–2019.

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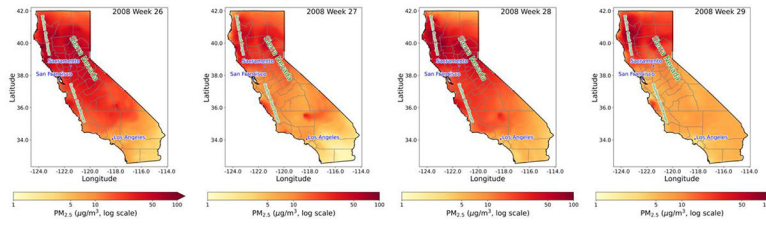
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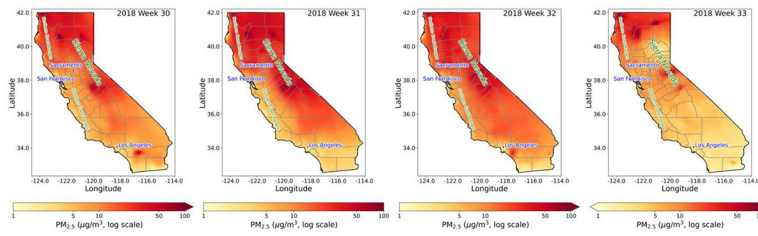


**Figure 2.**  
Estimated long-term average wildland fire PM<sub>2.5</sub> concentrations for 2007–2018.

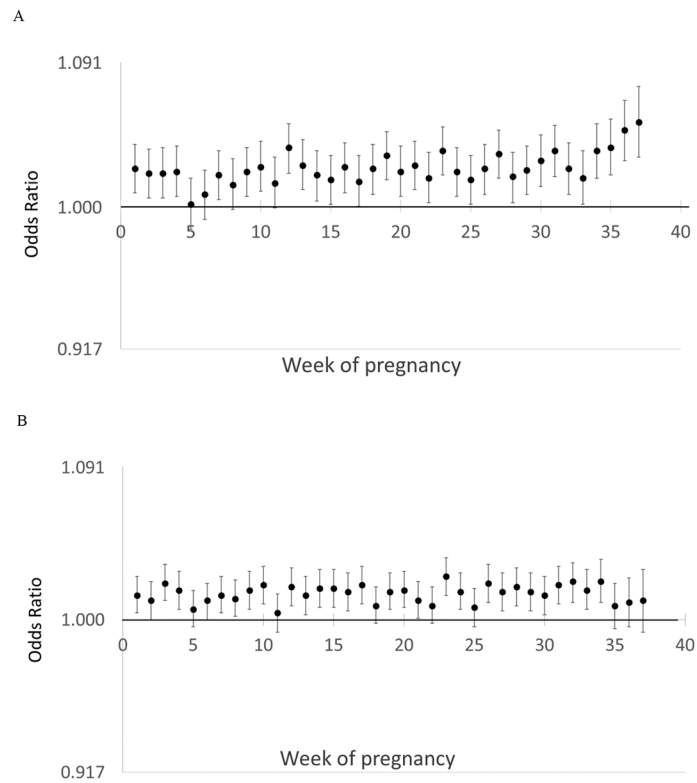




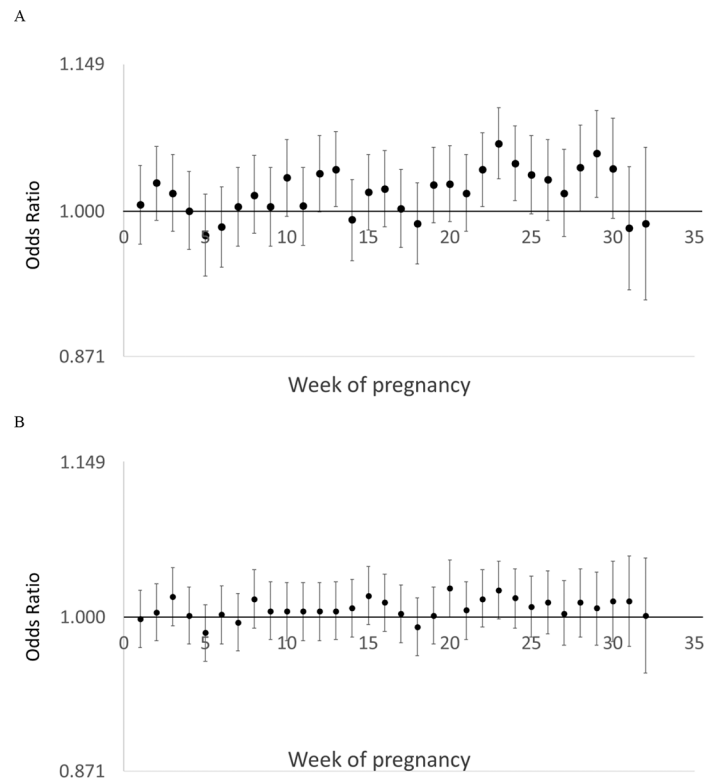
**Figure 3.** Estimated weekly average wildland fire  $PM_{2.5}$  concentrations for weeks 26–29 in 2008 (6/24/2008 – 7/21/2008) showing geographic and temporal variation in exposures during weeks with high fire activity.



**Figure 4.** Estimated weekly average wildland fire  $PM_{2.5}$  concentrations for weeks 30–33 in 2018 (7/23/2018 – 8/19/2018) showing geographic and temporal variation in exposures during weeks with high fire activity.



**Figure 5.** Odds ratios of eventual preterm birth (<37wks) (A) for 10µg/m<sup>3</sup> increase in wildland fire PM<sub>2.5</sub> exposure during each week of pregnancy and (B) comparing the highest to the lowest quartile of exposure to wildland fire PM<sub>2.5</sub>, among singleton births in California conceived 1/1/2007–12/31/2018. The odds ratios are presented on a logarithmic scale (base 2), with the axis going from 2<sup>-0.125</sup> to 2<sup>0.125</sup>.



**Figure 6.** Odds ratios of eventual early preterm birth (<32wks) (A) for 10µg/m<sup>3</sup> increase in wildland fire PM<sub>2.5</sub> exposure during each week of pregnancy and (B) comparing the highest to the lowest quartile of exposure to wildland fire PM<sub>2.5</sub>, among singleton births in California conceived 1/1/2007–12/31/2018. The odds ratios are presented on a logarithmic scale (base 2) with the range of values from 2<sup>-0.2</sup> to 2<sup>0.2</sup>.

**Table 1.**

Comparison of weekly leave one-out PM<sub>2.5</sub> concentration estimates to AQS observations by year in California.

Year	N	Mean Observed* (µg/m <sup>3</sup> )	Mean Estimated (µg/m <sup>3</sup> )	Mean Bias (µg/m <sup>3</sup> )	Mean Error (µg/m <sup>3</sup> )	Mean Fractional Bias (%)	Mean Fractional Error (%)	Coefficient of Determination (R <sup>2</sup> )
2007	5219	10.7	10	-0.7	3.5	-7	33	0.61
2008	5533	11.2	10.6	-0.6	3.2	-6	30	0.68
2009	5886	9.7	9.4	-0.3	3.1	-3	32	0.53
2010	6219	8.7	8.4	-0.3	2.8	-4	32	0.49
2011	6416	9.5	8.5	-0.9	3	-11	33	0.54
2012	6959	8.8	8.1	-0.7	2.7	-8	32	0.52
2013	6958	9.5	9.1	-0.4	2.9	-5	31	0.53
2014	7235	9	8.2	-0.8	2.8	-9	33	0.5
2015	7178	8.8	8.3	-0.5	2.6	-6	30	0.57
2016	7155	8.4	7.9	-0.5	2.4	-6	30	0.44
2017	7154	9.7	9.3	-0.4	2.9	-4	30	0.53
2018	7263	10.5	9.6	-0.9	3	-9	30	0.69
<b>average</b>		9.5	9.0	-0.6	2.9	-7	31	0.55

\* Based on observed daily concentrations greater than 1 µg/m<sup>3</sup>

**Table 2.**

Pregnancy average PM<sub>2.5</sub> exposure.

Year	Total PM <sub>2.5</sub> (µg/m <sup>3</sup> )	Non-fire PM <sub>2.5</sub> (µg/m <sup>3</sup> )	Wildland fire PM <sub>2.5</sub> (µg/m <sup>3</sup> )	Percent Wildland fire PM <sub>2.5</sub>
2007	10.8	9.9	0.9	9.0
2008	11.7	10.3	1.5	13.0
2009	11.3	10.4	1.0	8.3
2010	10.3	9.9	0.3	3.5
2011	9.4	9.2	0.2	2.7
2012	10.2	9.7	0.5	5.2
2013	9.8	9.2	0.6	6.5
2014	10.2	9.2	0.9	9.5
2015	9.7	9.0	0.7	7.5
2016	8.9	8.1	0.7	8.2
2017	9.1	8.1	1.0	11.3
2018	10.5	8.6	1.9	17.7
Average	10.2	9.3	0.9	8.5

**Table 3.** Characteristics of the cohort of singleton births in California by gestational age categories.

2007–2018	Early Preterm Birth (20–31 weeks)	Moderate/Late Preterm Birth (32–36 weeks)	Full term (37–44 weeks)			
	N	%	N	%		
<b>Number of births</b>	49219	1.0	305584	5.9	4800223	93.1
<b>Age of parent giving birth, years</b>						
<20	3778	7.7	20801	6.8	304635	6.3
20–24	9087	18.5	55369	18.1	921636	19.2
25–29	11796	24.0	75342	24.7	1288785	26.8
30–34	12773	26.0	82133	26.9	1343566	28.0
>=35	11785	23.9	71939	23.5	941601	19.6
<b>Education of parent giving birth</b>						
< high school	10674	21.7	64255	21.0	894884	18.6
high school/GED	14084	28.6	82378	27.0	1230117	25.6
some college	14239	28.9	82538	27.0	1247142	26.0
college degree or more	10222	20.8	76413	25.0	1428080	29.8
<b>Race/ethnicity of parent giving birth</b>						
White, non-Hispanic	9799	19.9	72604	23.8	1347120	28.1
Asian/Pacific Islander	6231	12.7	44273	14.5	695809	14.5
Black, non-Hispanic	5381	10.9	20337	6.7	234019	4.9
Hispanic	26097	53.0	159021	52.0	2383283	49.6
Other/unknown	1711	3.5	9349	3.1	139992	2.9
<b>Medical insurance: delivery</b>						
Medi-Cal	26171	53.2	154608	50.6	2266377	47.2
Private or other	23048	46.8	150976	49.4	2533846	52.8
<b>Cigarette smoking of parent giving birth</b>						
Ever smoker	2039	4.1	11122	3.6	127522	2.7
Never smoker	47180	95.9	294462	96.4	4672701	97.3
<b>Season of conception</b>						
Winter (Dec–Feb)	12866	26.1	78111	25.6	1237392	25.8
Spring (Mar–May)	12533	25.5	76409	25.0	1170997	24.4



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2007–2018	Early Preterm Birth (20–31 weeks)			Moderate/Late Preterm Birth (32–36 weeks)			Full term (37–44 weeks)			
	N	%	SD	N	%	SD	N	%	SD	
Year of birth	Summer (Jun–Aug)	11797	24.0	74048	24.2	1166680	24.3			
	Autumn (Sep–Nov)	12023	24.4	77016	25.2	1225154	25.5			
	2007	2075	4.2	9186	3.0	107121	2.2			
	2008	4421	9.0	29266	9.6	431678	9.0			
	2009	4192	8.5	26868	8.8	416225	8.7			
	2010	4076	8.3	26023	8.5	409908	8.5			
	2011	4143	8.4	25223	8.3	405156	8.4			
	2012	4130	8.4	25108	8.2	404104	8.4			
	2013	4163	8.5	24732	8.1	404301	8.4			
	2014	4136	8.4	24859	8.1	413056	8.6			
	2015	4078	8.3	24986	8.2	401680	8.4			
	2016	3946	8.0	24795	8.1	392070	8.2			
	2017	3862	7.8	24357	8.0	378447	7.9			
	2018	3761	7.6	23625	7.7	362208	7.5			
	2019	2236	4.5	16556	5.4	274269	5.7			
	<b>Average wildland fire PM<sub>2.5</sub></b>									
	Whole pregnancy	0.90	1.00	0.90	0.93	0.89	0.89			
	1st trimester	0.88	1.31	0.90	1.34	0.90	1.35			
	2nd trimester	0.91	1.36	0.90	1.36	0.88	1.35			
3rd trimester	0.93	2.40	0.92	1.66	0.91	1.49				
Any single pregnancy week	0.90	2.53	0.91	2.53	0.89	2.50				
<b>Average non-wildfire PM<sub>2.5</sub></b>										
Whole pregnancy	9.28	2.08	9.26	1.96	9.23	1.91				
1st trimester	9.34	2.61	9.33	2.59	9.30	2.57				
2nd trimester	9.23	2.60	9.22	2.57	9.19	2.54				
3rd trimester	9.23	3.66	9.23	2.89	9.18	2.65				
Any single pregnancy week	9.28	3.85	9.26	3.82	9.23	3.78				