

Prenatal Exposure to Wildfire and Autism in Children

David G. Luglio, Xin Yu, Jane C. Lin, Ting Chow, Mayra P. Martinez, Zhanghua Chen, Sandrah P. Eckel, Joel Schwartz, Frederick W. Lurmann, Nathan R. Pavlovic, Rob McConnell, Anny H. Xiang,^{*,○} and Md Mostafijur Rahman^{*,○}



Cite This: *Environ. Sci. Technol.* 2026, 60, 2907–2916



Read Online

ACCESS |



Metrics & More



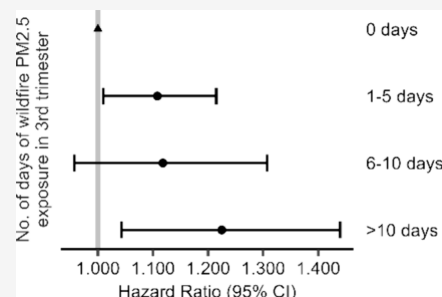
Article Recommendations



Supporting Information

ABSTRACT: Chronic health effects of wildfire $PM_{2.5}$ on neurodevelopmental outcomes are largely unknown. Therefore, the effects of wildfire $PM_{2.5}$ on autism were assessed in a southern California-based pregnancy cohort using Cox proportional hazard models. Exposure was estimated from 2006 to 2014 at maternal addresses across pregnancy and individual trimesters using three metrics: (1) mean wildfire $PM_{2.5}$ concentration, (2) number of days of smoke exposure, and (3) number of waves of smoke exposure. Analysis was restricted to days over specific $PM_{2.5}$ concentration thresholds (3 and 5 $\mu g/m^3$). Nonmovers during pregnancy (75% of cohort) were assessed in sensitivity analyses. There were 3356 autism diagnoses by age 5. Autism risk was associated with increased number of wildfire-exposed days during the third trimester and was strongest for nonmovers. Nonmover hazard ratios (HR) with exposure to 1–5, 6–10, and >10 wildfire days in the third trimester (compared to none) were 1.108 (95% CI: 1.010,1.215), 1.118 (0.957,1.307), and 1.225 (1.043,1.440), respectively. HR per wildfire wave increase (>3 $\mu g/m^3$ for 2 consecutive days) during the third trimester were 1.073 (1.009,1.140) and 1.267 (1.054,1.205) for the entire cohort and nonmovers, respectively. There was no association with the mean wildfire $PM_{2.5}$ concentration alone. Prenatal exposure to wildfire smoke may increase risk of autism among children.

KEYWORDS: wildfire, $PM_{2.5}$, autism, ASD, in utero, pregnancy, neurodevelopment



INTRODUCTION

The threat of wildfires to the environment and health is present and increasing across the United States. More areas are experiencing burned forest and grassland, especially in the west,^{1,2} with smoke emitted from these fires spreading over large swaths of the country.^{3–5} As a result, high-impact wildfire smoke days are becoming a concern continent-wide.⁶ In fact, expected reductions in total $PM_{2.5}$ concentrations from 2016 to 2022 as a result of regulation of man-made emissions sources of $PM_{2.5}$ have been partially reversed as a result of wildfires, a distinct source of $PM_{2.5}$, in many areas of the United States, including California.⁷

Autism (or autism spectrum disorder [ASD]) is a condition that is characterized by a range of divergent communicative, behavioral, and learning traits. Autistic individuals tend to have focused interests and discomfort with nonadherence to routines and may fail to recognize and understand social cues; in some cases, individuals may be nonverbal.^{8,9} Autism is caused by atypical neurodevelopment. It is known to have a major genetic contribution,¹⁰ but a large body of literature has shown an association between prenatal exposure to fine particulate matter ($PM_{2.5}$) air pollution and an increased risk of autism among children.^{11,12} We have reported increased autism risk associated with prenatal exposure to several $PM_{2.5}$ components, including elemental and organic carbons

and metals.^{13,14} Autism has been associated with several $PM_{2.5}$ sources, including tailpipe exhaust and residential heating.¹⁵

Wildfire $PM_{2.5}$ has a characteristic compositional profile; it is distinguished from other $PM_{2.5}$ sources by elevated concentrations of carbonaceous compounds, such as levoglucosan and polycyclic aromatic hydrocarbons (PAHs) like retene, as well as elements such as K, S, and some metals.^{3,16–20} Toxicity of PAHs and metals, in particular, have been well-described, including for neurological outcomes.^{21–23} $PM_{2.5}$ emissions from different sources have been shown to have different associations with autism.²⁴ A growing body of literature has demonstrated the acute effects of wildfire emitted particulate matter (PM) on several health outcomes.^{3,25–27} In particular, exposure to wildfire PM during pregnancy has been associated with decreased gestational age and birth weight,^{28–32} and neurological/cognitive effects in adults.^{33,34} While there are a growing number of studies with chronic effects of wildfire PM, there are none investigating associations with autism.^{35–37}

Received: June 18, 2025

Revised: December 5, 2025

Accepted: December 8, 2025

Published: January 20, 2026



Table 1. Characteristics of Mother–Child Pairs, With and without Autism Diagnosis

characteristics	children, no. (%) or median (interquartile range)		
	entire cohort (<i>n</i> = 204374)	autism-diagnosed (<i>n</i> = 3356)	nondiagnosed (<i>n</i> = 201018)
sex			
male (%)	104637 (51.2)	2694 (80.3)	101943 (50.7)
female (%)	99737 (48.8)	662 (19.7)	99075 (49.3)
maternal age at delivery, median [IQR ^a], years	30.6 [26.5, 34.4]	31.5 [27.8, 35.5]	30.6 [26.5, 34.4]
parity (<i>N</i> (%))			
0	70125 (34.3)	1332 (39.7)	68793 (34.2)
1	65458 (32.0)	1060 (31.6)	64398 (32.0)
≥2	50812 (24.9)	648 (19.3)	50164 (25.0)
unknown	17979 (8.8)	316 (9.4)	17663 (8.8)
maternal education (<i>N</i> (%))			
high school or lower	64658 (31.6)	920 (27.4)	63738 (31.7)
some college	62775 (30.7)	1110 (33.1)	61665 (30.7)
college graduate or higher	74619 (36.5)	1294 (38.6)	73325 (36.5)
unknown	2322 (1.1)	32 (1.0)	2290 (1.1)
household annual income ^b (<i>N</i> (%))			
<\$30,000	10368 (5.1)	159 (4.7)	10209 (5.1)
\$30,000–\$49,999	57578 (28.2)	993 (29.6)	56585 (28.1)
\$50,000–\$69,999	64296 (31.5)	1066 (31.8)	63230 (31.5)
\$70,000–\$89,999	40641 (19.9)	646 (19.2)	39995 (19.9)
>\$90,000	31491 (15.4)	492 (14.7)	30999 (15.4)
race/ethnicity (<i>N</i> (%))			
non-Hispanic white	50788 (24.9)	671 (20.0)	50117 (24.9)
non-Hispanic black	17465 (8.5)	300 (8.9)	17165 (8.5)
Hispanic	104085 (50.9)	1697 (50.6)	102388 (50.9)
Asian/Pacific Islander	27315 (13.4)	601 (17.9)	26714 (13.3)
other	4721 (2.3)	87 (2.6)	4634 (2.3)
any history of maternal comorbidity ^c (<i>N</i> (%))	35237 (17.2)	674 (20.1)	34563 (17.2)
prepregnancy diabetes ^d (<i>N</i> (%))	7731 (3.8)	190 (5.7)	7541 (3.8)
prepregnancy obesity ^e (<i>N</i> (%))	52231 (25.6)	1029 (30.7)	51202 (25.5)
year of birth (<i>N</i> (%))			
2006–2010	98628 (48.3)	1288 (38.4)	97340 (48.4)
2011–2014	105746 (51.7)	2068 (61.6)	103678 (51.6)

^aAbbreviations: IQR, interquartile range. ^bCensus tract level median household income. ^c≥1: diagnosis of heart, lung, kidney, or liver disease; cancer. ^dType I and Type II diabetes diagnosed before pregnancy. ^ePrepregnancy BMI ≥ 30.

Given the increasing impact of wildfire smoke on air quality, which may worsen with the changing climate, its impact on autism development warrants investigation.

The objective of this study was to investigate the effect of prenatal wildfire exposure on autism development in offspring, leveraging a large pregnancy cohort of the Kaiser Permanente Southern California healthcare system. Wildfire smoke PM_{2.5} concentrations were estimated by a state-of-the-art validated model.³⁸ We used several metrics of wildfire exposure including absolute wildfire PM_{2.5} concentration averaged over pregnancies and trimesters, number of days of wildfire events, and number of days of wildfire PM_{2.5} greater than 3 and 5 μg/m³, as previously suggested.³⁹

METHODS

Study Population

Participants were from a Kaiser Permanente Southern California (KPSC) pregnancy cohort, a group of mother–child pairs with singleton deliveries in system hospitals from January 1, 2006 through December 31, 2014. KPSC is an integrated healthcare system with over 4.5 million members whose membership is representative of the regional population.⁴⁰ Maternal sociodemographic data, pregnancy health

information, and addresses were extracted from KPSC's electronic medical records (EMR) system. Addresses were geocoded by using ArcGIS.

The cohort included 245902 singleton births from 2006 to 2014 who had continued KPSC membership after age 1; among them, 41210 pairs were removed due to missing/incomplete addresses. This included participant pairs with only a street name, locality, administrative unit, or 5-digit postal code since they could not provide a certain enough location for exposure assignment. Incomplete address information leads to exposure uncertainty and possible exposure misclassification since exposures vary spatially; imprecise address information may lead to inaccurate participant location assignment which may have different exposure estimates than the true location. In addition, 84 maternal/child pairs were excluded due to the maternal age of delivery being out-of-range (i.e., <15 years or >55 years), and 234 were excluded for missing or errors in covariates (e.g., birth weight, gender, maternal race–ethnicity, etc.). The final cohort size was 204374 mother–child pairs (Supporting Information Figure S1). Characteristics of this final group are given in Table 1.

Children were followed from birth until the diagnosis of autism, death, loss to follow-up, or age 5, whichever occurred first. Censoring at 5 years was done to ensure that each

participant had equivalent diagnosis periods. Screenings for autism diagnosis were administered at ages 18 and 24 months old during well-child visits for all children.⁴¹

Both KPSC (IRB No. 12075) and University of Southern California (IRB No. HS-20-00358) Institutional Review Boards approved this study with waivers of individual subject consent.

Autism Diagnosis

The end point of this study was the diagnosis or lack of diagnosis of autism spectrum disorder through the first 5 years of life. Diagnoses were identified by ICD-9 codes 299.0, 299.1, 299.8, and 299.9 (for EMR records before October 1, 2015) and ICD-10 codes F84.0, F84.3, F84.5, F84.8, and F84.9 (after October 1, 2015) at two or more visits, as previously described.^{41–44}

Exposure Assessment

The wildfire $PM_{2.5}$ concentration model has been described previously.³⁸ This model directly outputs daily wildfire smoke $PM_{2.5}$ concentrations on a 10×10 km² grid across the United States and has been used in other epidemiological investigations.^{5,45–48} Gradient boosted trees were fit to estimate wildfire $PM_{2.5}$ concentrations at all grid locations using satellite data, Hybrid Single-Particle Integrated Trajectory (HYSPLIT) model estimates, $PM_{2.5}$ concentrations measured at the EPA Air Quality System monitors (AQS), meteorological variables (e.g., directional wind speed, mean air temperature, etc.), distance to fires, and land-use and elevation data. The cross-validated R^2 value of this model was 0.67.

Daily wildfire $PM_{2.5}$ concentrations were assigned to the geocoded home address of each participant for the duration of each pregnancy, accounting for the change of address (as recorded in the EMR). Mean pregnancy and individual trimester concentrations were calculated for each individual and used in subsequent analysis. In addition, other measures of wildfire exposure were calculated, as previously recommended.³⁹ These include the number of days of nonzero wildfire $PM_{2.5}$ exposure and number of days of wildfire $PM_{2.5}$ exposure > 3 and > 5 $\mu\text{g}/\text{m}^3$ experienced by the participant at the home address. These thresholds represented the approximately 50th and 75th percentiles of wildfire exposure concentrations on wildfire days in this data set.

Additionally, daily averaged, 1 km resolution total $PM_{2.5}$ and O_3 concentrations were assigned to maternal addresses and averaged per individual trimester and over the entire pregnancy. Estimates were derived from an ensemble model described in detail elsewhere.^{49,50}

Covariates

Covariates included in this study were based on previously demonstrated associations and expert knowledge.^{43,51–53} Maternal-related variables included self-reported race/ethnicity, age at delivery, education, estimated household income based on census tract (per \$10000), and history of comorbidity (diagnosed heart, lung, kidney, or liver disease, or cancer; yes/no). Child-related covariates included sex, birth year, and indicator variables for season of conception (i.e., dry from April to October and wet from November to March in southern California). Birth year was included as a linear variable, given the increasing trend in autism diagnoses over time. Maternal prepregnancy diabetes mellitus (yes/no) and obesity (yes/no) were also included, as they are risk factors for autism,⁴¹ whereas low birth weight and gestational were not

included as they may be mediators in the causal pathway.^{29,30,32,54–56}

Statistical Analysis

Cox proportional hazard models estimated hazard ratios (HRs) for autism diagnosis associated with wildfire exposure metrics, adjusting for the above-mentioned covariates. For the wildfire $PM_{2.5}$ concentrations, HRs were estimated for the entire pregnancy and each of the three trimesters in a mutually adjusted trimester model. The associations with the number of days of exposure to any wildfire $PM_{2.5}$ and wildfire $PM_{2.5}$ concentrations above 3 and 5 $\mu\text{g}/\text{m}^3$ across the entire pregnancy and in the first, second, and third trimesters were evaluated. In another analysis, we created a four-level categorical variable based on the number of exposure days during pregnancy (0–5, 6–10, 11–20, and >20 days) and estimated autism risk using 0–5 days as the reference group. There were 82303 (40% of cohort), 36688 (18%), 71225 (35%), and 14158 (7%) participants in the respective categories, providing sufficient power to assess effects across these strata. Since wildfire exposure days per trimester were fewer than for the entire pregnancy, trimester-specific analyses categorized wildfire exposure as 0, 1–5, 6–10, and >10 days, with 0 days as the reference group. Similar analyses were conducted for the wildfire $PM_{2.5}$ concentrations > 3 and > 5 $\mu\text{g}/\text{m}^3$ with categories of 0–5, 6–10, and >10 days of exposure for both pregnancy and trimesters (reduced to three-level categorical variables to maintain sufficient power). Finally, to assess whether there was an effect of being exposed to continuous periods of wildfire, we assessed whether increased frequencies of waves of wildfire were associated with autism risk. These waves were defined over two duration periods (i.e., 2 consecutive days or more of exposure and 3 consecutive days or more of exposure) across three wildfire $PM_{2.5}$ thresholds (i.e., >0 , >3 , and >5 $\mu\text{g}/\text{m}^3$) for a total of six exposures (e.g., 2 days, >0 $\mu\text{g}/\text{m}^3$; 2 days, >3 $\mu\text{g}/\text{m}^3$; 3 days, >0 $\mu\text{g}/\text{m}^3$; 3 days, >5 $\mu\text{g}/\text{m}^3$).

Although we had access to information about residential moves during pregnancy in the EMR, we did not know the exact date and reason for the moves. Therefore, we used the midpoint between EMR-recorded address changes as the date of move and corresponding change in exposure. Fortunately, medical visits during pregnancy are frequent, but some exposure misclassification of movers is likely to have occurred. Therefore, we conducted analyses for the entire cohort and separately for mother–child pairs who did not change residential addresses during pregnancy (nonmovers), for whom exposure misclassification would have been reduced. We hypothesized that associations would be stronger among nonmovers due to reduced exposure misclassification. Summary of exposure metrics is presented in Table S1.

To address the effects of other pollutants, we adjusted the models with pregnancy or trimester averages of O_3 concentrations or remainder $PM_{2.5}$ concentrations. Remainder $PM_{2.5}$ values were calculated as total $PM_{2.5}$ minus wildfire $PM_{2.5}$. Additionally, to adjust for potential spatial confounding effects, an indicator variable for the medical center of treatment was included as a categorical variable in the model as a sensitivity analysis.

For the analysis with absolute wildfire $PM_{2.5}$ exposure, we scaled the HRs per pregnancy IQR increase in concentrations. For the analysis with the number of wildfire exposure days, we scaled HRs per unit day of increased exposure. Finally, for

Table 2. Wildfire Exposure Characteristics of Cohort over Pregnancy and Individual Trimesters

		pregnancy	1st trimester	2nd trimester	3rd trimester
wildfire PM _{2.5} concn (μg/m ³) ^a	mean (SD) ^c	0.18 (0.21)	0.18 (0.38)	0.18 (0.36)	0.18 (0.39)
	median (IQR) ^d	0.10 (0.21)	0.04 (0.15)	0.05 (0.16)	0.05 (0.16)
no. of wildfire smoke days ^b	mean (SD)	9.55 (6.89)	3.14 (4.16)	3.42 (4.35)	2.99 (3.98)
	median (IQR)	8 (13)	1 (4)	2 (4)	1 (4)
no. of wildfire smoke days > 3 μg/m ³ ^b	mean (SD)	4.83 (4.65)	1.60 (2.82)	1.71 (2.92)	1.52 (2.71)
	median (IQR)	3 (7)	0 (2)	0 (2)	0 (2)
no. of wildfire smoke days > 5 μg/m ³	mean (SD)	2.78 (3.50)	0.93 (2.09)	0.99 (2.15)	0.87 (2.00)
	median (IQR)	1 (4)	0 (1)	0 (1)	0 (1)

^aWildfire PM_{2.5} concentrations are averaged per individual across each period including non-wildfire days (where concentrations are 0 μg/m³).
^bNote that the number of smoke days is inclusive of the number of smoke days > 3 μg/m³ and > 5 μg/m³, as number of smoke days > 3 μg/m³ are inclusive of number of smoke days > 5 μg/m³. ^cSD, standard deviation. ^dIQR, interquartile range.

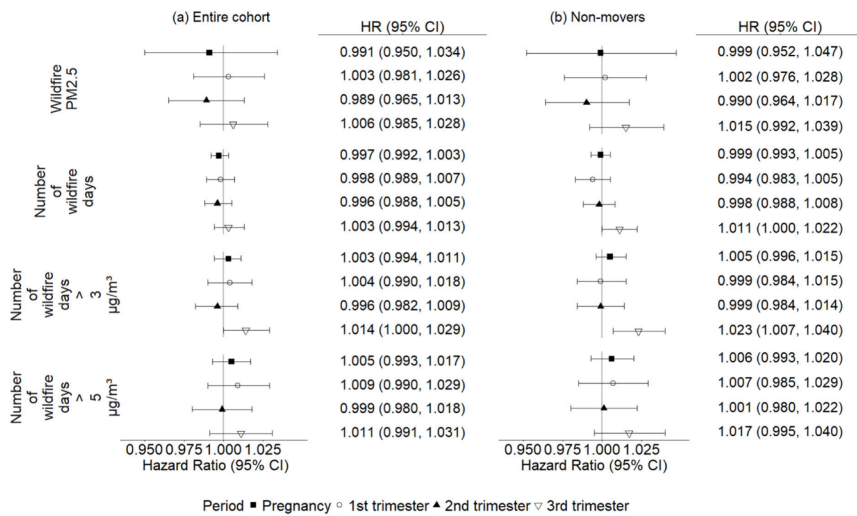


Figure 1. Hazard ratios between wildfire smoke exposure during entire pregnancy and each trimester and autism diagnosis in the (a) entire and (b) nonmover subsets of the cohort. PM_{2.5} concentrations are scaled per pregnancy IQR (0.21 μg/m³), and the number of days of exposure are scaled per day. Shapes indicate the HR for the particular period, and the bars represent the 95% confidence intervals (CIs).

wave analysis, we scaled HRs per unit wave of increased exposure.

All statistical analyses were performed in R (version 3.5⁵⁷) with packages Survival⁵⁸ and HeatWaveR⁵⁹ for creation of wildfire waves.

RESULTS

Population Demographics

Characteristics of the study population are listed in Table 1. Mothers with autism-diagnosed children tended to be older and nulliparous and had a higher prevalence of prepregnancy diabetes and obesity. There were four times as many boys diagnosed with autism as girls. The median age of autism diagnosis in this cohort was 3.3 years. Characteristics of the nonmover (75% of total) and mover populations (25% of total) are listed in Table S2. Nonmovers were slightly older and more parous than the entire cohort and the mover population, with greater proportions of college graduates and higher prevalence of comorbidities, including prepregnancy diabetes and obesity. There were slightly higher census-tract income levels in the nonmover group.

Exposures

About 60% of mother–child pairs were exposed to more than 5 days of wildfire smoke PM during pregnancy (Table S3). The mean exposure concentration for the cohort was 0.18 μg/

m³ (Table 2), and the median number of days of exposure was 8, indicating that exposure was relatively infrequent. Exposure to exceptionally high concentrations of wildfire PM_{2.5} was rare (i.e., median days of exposure to wildfire PM_{2.5} concentrations > 5 μg/m³ was 1). Exposure levels for movers and nonmovers are presented in Table S4. These indicate that nonmovers were exposed to overall higher concentrations and greater number of days of wildfire PM_{2.5}. This was consistent when averaging over the entire pregnancy, over individual trimesters, or by a wildfire event day. Exposure to wildfire waves during pregnancy and each trimester are summarized in Table S5. About 70% of participants were exposed to a 2 day wildfire PM_{2.5} event during their pregnancy.

Associations with Autism

We did not find an association between the average wildfire PM_{2.5} mass concentration and autism (Figure 1a). There was an association with increased numbers of days of exposure to wildfire PM_{2.5} > 3 μg/m³ in the third trimester (HR [CI]: 1.014 [1.000, 1.029] per 1 day increase). Additional significant results were observed when the number of days was categorized into different levels (Table S6). Children exposed to 1–5 days of any wildfire PM_{2.5} during the third trimester had elevated risk of autism compared to those not exposed (0 days) at all (HR [CI]: 1.085 [1.002, 1.176]). The effect size was larger for wildfire PM_{2.5} > 3 μg/m³ (HR [CI]: 1.178 [1.018, 1.362]). Adjustment for the medical center, total

PM_{2.5}, and O₃ did not appreciably change the results (Tables S7 and S8).

When restricting the cohort to nonmovers these effects strengthened. This is apparent for increases in total days of any exposure (HR [CI]: 1.011 [1.000, 1.022]) or days with wildfire PM_{2.5} concentrations > 3 μg/m³ (1.023 [1.007, 1.040]) in the third trimester (Figure 1b). The results for the analyses with categorized wildfire exposure days are shown in Figure 2 and

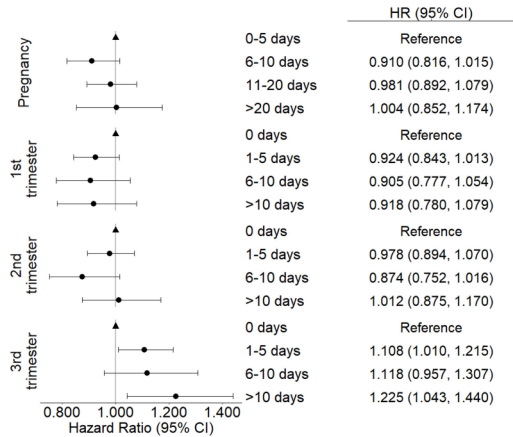


Figure 2. Hazard ratios for nonmovers categorized by the number of days of any wildfire PM_{2.5} exposure for each trimester. Shapes indicate the HR, with the triangle representing the reference group, and the bars represent the 95% confidence intervals (CIs).

Figures S2 and S3. There was a significant increase in autism risk among mother–child pairs who were exposed to wildfire during the third trimester compared to those not exposed at all (Figure 2). The HRs of autism for exposure to 1–5, 6–10, and >10 days of wildfire, compared to none, were 1.108 (1.010, 1.215), 1.118 (0.957, 1.307), and 1.225 (1.043, 1.440), respectively. With the threshold of wildfire PM_{2.5} > 3 μg/m³, we also found a significant increase in autism risk associated with increased wildfire exposure days in the third trimester (Figure S2). No association was observed in the entire pregnancy, first, or second trimester analyses.

Increases in the continuous number of days of exposure to wildfire PM_{2.5} > 5 μg/m³ did not show any significant

associations; associations, however, were found in analysis with categorized levels of wildfire exposure days (Figure S3). Nonmover pairs exposed to over 10 days of wildfire PM_{2.5} > 5 μg/m³, over the entire pregnancy period, had a HR of 1.277 (1.043, 1.5621) compared with pairs exposed to five or fewer days of wildfire PM_{2.5} > 5 μg/m³.

The results of the analysis with wildfire exposure waves, which combined both the duration and intensity, are presented in Table 3. In the full cohort, when defining an occurrence of wildfire wave as at least two consecutive days of wildfire PM_{2.5} over 3 or 5 μg/m³, increased frequencies of waves during pregnancy were significantly associated with autism risk (HR [CI]: 1.045 [1.009, 1.081] and 1.057 [1.008, 1.108], respectively). Strong associations for 2 day waves were observed in the third trimester for both the entire cohort and among nonmovers. Analysis by 3 day waves yielded similar results. There were significant pregnancy-wide associations for the cohort for increases in 3 day waves of wildfire PM_{2.5} > 0 μg/m³ (entire cohort: 1.037 [1.003, 1.072]; nonmovers: 1.049 [1.011, 1.090]), but none for 3 day waves of wildfire PM_{2.5} > 5 μg/m³ across pregnancy and all trimester periods.

DISCUSSION

This study was the first to examine the effect of prenatal exposure to wildfire on autism. The association between wildfire and autism diagnosis in offspring was assessed by utilizing a large multiethnic population-based pregnancy cohort in Southern California and a well-validated, state-of-the-art wildfire PM_{2.5} model.³⁸ Increased number of days of any exposure to wildfire were associated with autism, especially in the third trimester, and the effects sizes were greater among nonmovers, although these effect sizes were small to moderate (HR up to 1.13). There was increased autism risk associated with increased frequencies of 2 day and 3 day waves of exposure across the full pregnancy and third trimester in the full cohort, and these effect estimates were stronger among nonmovers. Compared to the 2 day wave analysis, 3 day wave results show an increased effect size across the pregnancy and third trimesters for the >0 and >3 μg/m³ thresholds, which may be indicative of a dose–response. The lack of associations for 3 day waves of wildfire PM_{2.5} > 5 μg/m³, however, limits this interpretation.

Table 3. Hazard Ratios (HRs) between Exposure to Wildfire Waves and Autism Risk in the Entire Cohort and Subset of Nonmovers

	HR (95% confidence interval)			
	pregnancy	1st trimester	2nd trimester	3rd trimester
entire cohort (<i>n</i> = 204374)				
2 days, >0 μg/m ³	1.005 (0.983, 1.028)	1.000 (0.960, 1.042)	1.000 (0.963, 1.038)	1.029 (0.986, 1.073)
2 days, >3 μg/m ³	1.045 (1.009, 1.081)	1.042 (0.984, 1.103)	1.027 (0.971, 1.087)	1.076 (1.012, 1.144)
2 days, >5 μg/m ³	1.057 (1.008, 1.108)	1.068 (0.987, 1.155)	1.038 (0.959, 1.124)	1.083 (0.999, 1.174)
3 days, >0 μg/m ³	1.037 (1.003, 1.072)	1.036 (0.975, 1.100)	1.025 (0.969, 1.085)	1.061 (0.997, 1.128)
3 days, >3 μg/m ³	1.054 (1.002, 1.109)	1.078 (0.992, 1.172)	1.027 (0.944, 1.118)	1.077 (0.985, 1.177)
3 days, >5 μg/m ³	1.023 (0.957, 1.094)	1.033 (0.924, 1.156)	1.009 (0.900, 1.131)	1.045 (0.926, 1.178)
nonmovers (<i>n</i> = 154036)				
2 days, >0 μg/m ³	1.015 (0.990, 1.041)	0.985 (0.940, 1.032)	1.006 (0.964, 1.049)	1.079 (1.029, 1.131)
2 days, >3 μg/m ³	1.068 (1.087, 1.127)	1.033 (0.968, 1.102)	1.053 (0.990, 1.122)	1.133 (1.059, 1.212)
2 days, >5 μg/m ³	1.075 (1.020, 1.133)	1.078 (0.988, 1.177)	1.045 (0.957, 1.141)	1.127 (1.030, 1.233)
3 days, >0 μg/m ³	1.049 (1.011, 1.090)	1.008 (0.941, 1.081)	1.038 (0.974, 1.107)	1.123 (1.049, 1.203)
3 days, >3 μg/m ³	1.077 (1.018, 1.139)	1.071 (0.975, 1.177)	1.047 (0.953, 1.151)	1.137 (1.030, 1.254)
3 days, >5 μg/m ³	1.050 (0.974, 1.131)	1.075 (0.948, 1.218)	1.014 (0.892, 1.152)	1.083 (0.946, 1.239)

A smaller sample size and reduced power among higher exposure thresholds (i.e., $5 \mu\text{g}/\text{m}^3$ or >10 days exposure for the categorical assignments) may explain the lack of a consistent dose–response. For example, only 8% of the cohort was exposed to 10 days or more of wildfire $\text{PM}_{2.5} > 3 \mu\text{g}/\text{m}^3$ in the third trimester. Alternatively, more severe wildfire events, marked by higher $\text{PM}_{2.5}$ concentrations, may result in evacuation and temporary relocation or use of indoor particle filters that could result in exposure misclassification. A previous study found that, on moderate smoke days, people stayed at home.⁶⁰ On severe smoke days, people were more likely to temporarily relocate. Information about whether the participants temporarily relocated during a wildfire event or used indoor air filters was not available.

Estimates of effects were larger in the nonmovers than in the entire cohort. Movers likely have greater rates of exposure misclassification since dates of residential moves were interpolated between dates with different addresses. Change in address may also be linked to the presence of fires. Although we do not have information on the reason for moving, those with frequent fire exposure may choose to move. That movers were exposed to a lower average concentration and fewer days of wildfire $\text{PM}_{2.5}$ provides some plausibility to this hypothesis. It is unclear whether other differences in characteristics between the mover and nonmover groups explained the differences between the entire cohort and nonmovers. The nonmover population was older, more parous, and more highly educated than the mover population; however, we adjusted for these covariates.

Previous studies reported associations between autism and $\text{PM}_{2.5}$ concentrations across different pregnancy windows,^{11,61} including the first and the second and the third trimesters.^{12,62,63} In this cohort we previously found larger effects of $\text{PM}_{2.5}$ (from all sources) in the first trimester.¹² This study suggests that there is a window of susceptibility to wildfire exposure in the third trimester. Possible reasons for this different wildfire window of susceptibility are not clear. Differences in patterns of exposure and wildfire PM composition and toxicity, which are different from ambient PM from other sources, may play some role. In contrast to wildfire $\text{PM}_{2.5}$, usual ambient $\text{PM}_{2.5}$ concentrations are chronic at low to moderate levels; wildfire exposures are characterized by intermittent, high-concentration spikes. Increasing neuronal connectivity and organization and rapid gray matter growth are characteristic of third trimester fetal brain development^{64,65} and may be more strongly affected when there are high acute exposures. It is also plausible that there is an increased susceptibility to specific components or the compositional profile of wildfire PM during certain periods. Composition of wildfires burning at the urban interface reflects burning structures with highly toxic and poorly characterized pyrolysis products with unknown trimester-specific effects.¹⁷ Wildfire smoke has been reported to be enriched in K, S, Al, Si, and carbonaceous material.^{3,16,18} Carbonaceous PM components have been previously associated with autism development.^{13,66} Wildfire $\text{PM}_{2.5}$ also generates reactive oxygen species with oxidative potential.^{67,68} Finally, wildfire smoke PM has been associated with preterm birth, and the strongest effects of increasing days of exposure were in the later pregnancy.³⁰ Preterm birth, which is associated with autism, is a potential third trimester mediator of wildfire smoke exposure and autism, although other studies of preterm birth and wildfire

exposure have not identified consistent trimester-specific effects.^{28,29}

It is also possible that other mediators may have caused the observed associations. Wildfire events, for example, have been associated with bouts of mental health stress, including anxiety and depression,^{69–72} maternal stress during pregnancy has been associated with autism development⁷³ in their children. Accordingly, these wildfire exposures may be linked to autism through stress as a mediator. Although we had adjusted for O_3 and remainder $\text{PM}_{2.5}$, other component or source-specific air pollution such as heavy metals could be potential confounders^{13,14,24} but were not considered. In addition, plausibly confounding temperature effects were not analyzed. Finally, other unmeasured variables, such as maternal/household activity, which could modify our findings, should be considered in future work.

No association was observed between mean wildfire $\text{PM}_{2.5}$ concentrations and rates of autism diagnosis in this cohort across all exposure windows. These results are plausibly consistent with previous investigation examining other source-specific estimates of $\text{PM}_{2.5}$ from a chemical transport model in this cohort; we found no association between mean biomass combustion $\text{PM}_{2.5}$ and autism.²⁴

We did not adjust for multiple testing. The wildfire exposure metrics were selected to represent different complementary features of the same underlying exposure. Notably, the statistically significant findings were concentrated in the third-trimester analyses and, more specifically, in the number of smoke-day exposures. This pattern both temporally specific (third trimester) and exposure-specific (smoke days) argues against random false positives. Moreover, the third-trimester association with smoke-day count was replicated across three analytic specifications (continuous number of smoke days, four-level categorical variable for smoke-day count, and the “wildfire wave” metric that integrates concentration and duration), which further reduces the likelihood that the result is a false discovery.

This study used a large, well-established cohort with a high retention and state-of-the-art wildfire $\text{PM}_{2.5}$ exposure model in a region of the United States where wildfires are common and likely to increase in frequency and intensity because of climate change. Using different definitions of exposure allowed for a more robust analysis of the associations between wildfire and autism development. Some limitations include potential exposure misclassification of participants who may have evacuated during wildfire events and use of indoor air filters or personal protective equipment. Unmeasured mediators such as psychosocial stress may also have explained some of associations of exposure with autism. A variety of other potentially confounding variables, such as other source-specific or component-specific PM or other air pollutants were not included. Future work should apply multipollutant models to disentangle the independent effects of each pollutant.

Prenatal wildfire exposure was associated with autism risk in a large KPSC cohort across multiple corroborative analyses. Associations were generally strongest in the third trimester and in nonmovers, suggesting there may be a window of susceptibility during late-stage pregnancy. Further research is needed to replicate these findings, to clarify some uncertainties in the dose–response, and to identify biological pathways responsible for the associations. Public health authorities may consider prioritizing pregnant women for protection from wildfire smoke, perhaps particularly during late pregnancy.

■ ASSOCIATED CONTENT

Data Availability Statement

KPSC Institutional Review Board approved this study, with waiver of informed consent with the condition that raw data remain confidential and would not be shared. Thus, due to the sensitive nature of these data, the data are not available to be shared.

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.est.5c08256>.

Summary of exposure metrics, additional demographic and exposure information about the cohort, and additional results for smoke day count associations and sensitivity analysis (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Md Mostafijur Rahman – Department of Environmental Health Sciences, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana 70118, United States; orcid.org/0000-0002-2405-3276; Email: mrahman8@tulane.edu

Anny H. Xiang – Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California 91101, United States; orcid.org/0000-0003-2786-1268; Email: anny.h.xiang@kp.org

Authors

David G. Luglio – Department of Environmental Health Sciences, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana 70118, United States; orcid.org/0000-0003-4669-547X

Xin Yu – Department of Environmental Medicine, Icahn School of Medicine at Mount Sinai, New York, New York 10029, United States

Jane C. Lin – Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California 91101, United States

Ting Chow – Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California 91101, United States

Mayra P. Martinez – Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California 91101, United States

Zhanghua Chen – Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, California 90089, United States

Sandra P. Eckel – Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, California 90089, United States

Joel Schwartz – Department of Environmental Health and Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, Massachusetts 02115, United States

Frederick W. Lurmann – Sonoma Technology, Inc., Petaluma, California 94954, United States; orcid.org/0000-0001-9943-4172

Nathan R. Pavlovic – Sonoma Technology, Inc., Petaluma, California 94954, United States; orcid.org/0000-0003-2127-3940

Rob McConnell – Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, California 90089, United States

Complete contact information is available at:

<https://pubs.acs.org/doi/10.1021/acs.est.5c08256>

Author Contributions

○M.M.R. and A.H.X. contributed equally to this work.

Funding

This study was supported by National Institutes of Environmental Health Sciences (R01 ES029963 (A.H.X., R.M., and M.M.R.); R56ES028121 (A.H.X.); P30ES007048 and P2CES033433 (R.M.), and by Kaiser Permanente Southern California Direct Community Benefit Funds. J.S. was supported by EPA Grant RD-835872.

Notes

Disclosures. A.H.X. had full access to all of the data in the study. D.G.L., A.H.X., and M.M.R. take responsibility for the integrity of the data and the accuracy of the data analysis. J.S. has testified on behalf of the U.S. Department of Justice in a case involving a Clean Air Act violation. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the patients of Kaiser Permanente for helping us improve care through the use of information collected through our electronic health record systems, and the Kaiser Permanente and the Utility for Care Data Analysis (UCDA) team within Kaiser Permanente for creating the GEMS Datamart with consolidated addresses histories available to facilitate our research.

■ REFERENCES

- (1) Radeloff, V. C.; Mockrin, M. H.; Helmers, D.; Carlson, A.; Hawbaker, T. J.; Martinuzzi, S.; Schug, F.; Alexandre, P. M.; Kramer, H. A.; Pidgeon, A. M. Rising wildfire risk to houses in the United States, especially in grasslands and shrublands. *Science* **2023**, 382 (6671), 702–7.
- (2) Li, S.; Banerjee, T. Spatial and temporal pattern of wildfires in California from 2000 to 2019. *Scientific Reports* **2021**, 11 (1), 8779.
- (3) Thurston, G.; Yu, W.; Luglio, D. An Evaluation of the Asthma Impact of the June 2023 New York City Wildfire Air Pollution Episode. *Am. J. Respir. Crit. Care Med.* **2023**, 208 (8), 898–900.
- (4) Burke, M.; Driscoll, A.; Heft-Neal, S.; Xue, J.; Burney, J.; Wara, M. The changing risk and burden of wildfire in the United States. *Proceedings of the National Academy of Sciences* **2021**, 118 (2), No. e2011048118.
- (5) Wen, J.; Heft-Neal, S.; Baylis, P.; Boomhower, J.; Burke, M. Quantifying fire-specific smoke exposure and health impacts. *Proceedings of the National Academy of Sciences* **2023**, 120 (51), No. e2309325120.
- (6) D'Evelyn, S. M.; Jung, J.; Alvarado, E.; Baumgartner, J.; Caligiuri, P.; Hagmann, R. K.; Henderson, S. B.; Hessburg, P. F.; Hopkins, S.; Kasner, E. J.; Krawchuk, M. A.; Krenz, J. E.; Lydersen, J. M.; Marlier, M. E.; Masuda, Y. J.; Metlen, K.; Mittelstaedt, G.; Prichard, S. J.; Schollaert, C. L.; Smith, E. B.; Stevens, J. T.; Tessum, C. W.; Reeb-Whitaker, C.; Wilkins, J. L.; Wolff, N. H.; Wood, L. M.; Haugo, R. D.; Spector, J. T. Wildfire, Smoke Exposure, Human Health, and

Environmental Justice Need to be Integrated into Forest Restoration and Management. *Curr. Environ. Health Rep.* **2022**, 9 (3), 366–85.

(7) Burke, M.; Childs, M. L.; de la Cuesta, B.; Qiu, M.; Li, J.; Gould, C. F.; Heft-Neal, S.; Wara, M. The contribution of wildfire to PM_{2.5} trends in the USA. *Nature* **2023**, 622 (7984), 761–6.

(8) Lord, C.; Elsabbagh, M.; Baird, G.; Veenstra-Vanderweele, J. Autism spectrum disorder. *Lancet* **2018**, 392 (10146), 508–20.

(9) American Psychological Association. *Neurodevelopmental Disorders. Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., text rev. ed.; American Psychiatric Association: Arlington, VA, 2022.

(10) Eyring, K. W.; Geschwind, D. H. Three decades of ASD genetics: building a foundation for neurobiological understanding and treatment. *Hum. Mol. Genet.* **2021**, 30 (20), R236–R44.

(11) Lin, C.-K.; Chang, Y.-T.; Lee, F.-S.; Chen, S.-T.; Christiani, D. Association between exposure to ambient particulate matters and risks of autism spectrum disorder in children: a systematic review and exposure-response meta-analysis. *Environmental Research Letters* **2021**, 16 (6), 063003.

(12) Rahman, M. M.; Shu, Y.-H.; Chow, T.; Lurmann, F. W.; Yu, X.; Martinez, M. P.; Carter, S. A.; Eckel, S. P.; Chen, J.-C.; Chen, Z.; Levitt, P.; Schwartz, J.; McConnell, R.; Xiang, A. H. Prenatal Exposure to Air Pollution and Autism Spectrum Disorder: Sensitive Windows of Exposure and Sex Differences. *Environmental Health Perspectives* **2022**, 130 (1), 017008.

(13) Rahman, M. M.; Carter, S. A.; Lin, J. C.; Chow, T.; Yu, X.; Martinez, M. P.; Chen, Z.; Chen, J. C.; Rud, D.; Lewinger, J. P.; van Donkelaar, A.; Martin, R. V.; Eckel, S. P.; Schwartz, J.; Lurmann, F.; Kleeman, M. J.; McConnell, R.; Xiang, A. H. Associations of Autism Spectrum Disorder with PM_{2.5} Components: A Comparative Study Using Two Different Exposure Models. *Environ. Sci. Technol.* **2023**, 57 (1), 405–14.

(14) Rahman, M. M.; Carter, S. A.; Lin, J. C.; Chow, T.; Yu, X.; Martinez, M. P.; Levitt, P.; Chen, Z.; Chen, J. C.; Rud, D.; Lewinger, J. P.; Eckel, S. P.; Schwartz, J.; Lurmann, F. W.; Kleeman, M. J.; McConnell, R.; Xiang, A. H. Prenatal exposure to tailpipe and non-tailpipe tracers of particulate matter pollution and autism spectrum disorders. *Environ. Int.* **2023**, 171, 107736.

(15) Flanagan, E.; Malmqvist, E.; Rittner, R.; Gustafsson, P.; Källén, K.; Oudin, A. Exposure to local, source-specific ambient air pollution during pregnancy and autism in children: a cohort study from southern Sweden. *Scientific Reports* **2023**, 13 (1), 3848.

(16) Sparks, T. L.; Wagner, J. Composition of particulate matter during a wildfire smoke episode in an urban area. *Aerosol Sci. Technol.* **2021**, 55 (6), 734–47.

(17) Jaffe, D. A.; O'Neill, S. M.; Larkin, N. K.; Holder, A. L.; Peterson, D. L.; Halofsky, J. E.; Rappold, A. G. Wildfire and prescribed burning impacts on air quality in the United States. *Journal of the Air & Waste Management Association* **2020**, 70 (6), 583–615.

(18) Balachandran, S.; Pachon, J. E.; Lee, S.; Oakes, M. M.; Rastogi, N.; Shi, W.; Tagaris, E.; Yan, B.; Davis, A.; Zhang, X.; Weber, R. J.; Mulholland, J. A.; Bergin, M. H.; Zheng, M.; Russell, A. G. Particulate and gas sampling of prescribed fires in South Georgia, USA. *Atmos. Environ.* **2013**, 81, 125–35.

(19) Alves, C.; Vicente, A.; Nunes, T.; Gonçalves, C.; Fernandes, A. P.; Mirante, F.; Tarelho, L.; Sánchez de la Campa, A. M.; Querol, X.; Caseiro, A.; Monteiro, C.; Evtyugina, M.; Pio, C. Summer 2009 wildfires in Portugal: Emission of trace gases and aerosol composition. *Atmos. Environ.* **2011**, 45 (3), 641–9.

(20) Boaggio, K.; LeDuc, S. D.; Rice, R. B.; Duffney, P. F.; Foley, K. M.; Holder, A. L.; McDow, S.; Weaver, C. P. Beyond Particulate Matter Mass: Heightened Levels of Lead and Other Pollutants Associated with Destructive Fire Events in California. *Environ. Sci. Technol.* **2022**, 56 (20), 14272–83.

(21) Mille, T.; Graindorge, P. H.; Morel, C.; Paoli, J.; Lichtfouse, E.; Schroeder, H.; Grova, N. The overlooked toxicity of non-carcinogenic polycyclic aromatic hydrocarbons. *Environmental Chemistry Letters* **2024**, 22 (4), 1563–7.

(22) Xu, P.; Liu, B.; Chen, H.; Wang, H.; Guo, X.; Yuan, J. PAHs as environmental pollutants and their neurotoxic effects. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology* **2024**, 283, 109975.

(23) Lopes de Andrade, V.; Marreilha dos Santos, A. P.; Aschner, M. Neurotoxicity of metal mixtures. In *Advances in Neurotoxicology*, Vol. 5; Aschner, M., Costa, L. G., Eds.; Academic Press, 2021; Chapter 11, pp 329–64. DOI: 10.1007/978-3-319-60189-2_12.

(24) Luglio, D.; Kleeman, M.; Yu, X.; Lin, J.; Chow, T.; Martinez, M.; Chen, Z.; Chen, J.-C.; Eckel, S.; Schwartz, J.; Lurmann, F.; McConnell, R.; Xiang, A.; Rahman, M. M. Prenatal Exposure to Source-Specific Fine Particulate Matter and Autism Spectrum Disorder. *Environmental Science & Technology* **2024**, 58, 18566–77.

(25) Aguilera, R.; Corringham, T.; Gershunov, A.; Benmarhnia, T. Wildfire smoke impacts respiratory health more than fine particles from other sources: observational evidence from Southern California. *Nature Communications* **2021**, 12 (1), 1493.

(26) Chen, K.; Ma, Y.; Bell, M. L.; Yang, W. Canadian Wildfire Smoke and Asthma Syndrome Emergency Department Visits in New York City. *JAMA* **2023**, 330 (14), 1385–7.

(27) Korsiak, J.; Pinault, L.; Christidis, T.; Burnett, R. T.; Abrahamowicz, M.; Weichenthal, S. Long-term exposure to wildfires and cancer incidence in Canada: a population-based observational cohort study. *The Lancet Planetary Health* **2022**, 6 (5), e400–e9.

(28) Abdo, M.; Ward, I.; O'Dell, K.; Ford, B.; Pierce, J. R.; Fischer, E. V.; Crooks, J. L. Impact of Wildfire Smoke on Adverse Pregnancy Outcomes in Colorado, 2007–2015. *International Journal of Environmental Research and Public Health* **2019**, 16 (19), 3720.

(29) Zhang, Y.; Ye, T.; Yu, P.; Xu, R.; Chen, G.; Yu, W.; Song, J.; Guo, Y.; Li, S. Preterm birth and term low birth weight associated with wildfire-specific PM_{2.5}: A cohort study in New South Wales, Australia during 2016–2019. *Environment International* **2023**, 174, 107879.

(30) 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**, 203, 111872.

(31) Picciotto, S.; Huang, S.; Lurmann, F.; Pavlovic, N.; Ying Chang, S.; Mukherjee, A.; Goin, D. E.; Sklar, R.; Noth, E.; Morello-Frosch, R.; Padula, A. M. Pregnancy exposure to PM_{2.5} from wildland fire smoke and preterm birth in California. *Environ. Int.* **2024**, 186, 108583.

(32) Requia, W. J.; Amini, H.; Adams, M. D.; Schwartz, J. D. Birth weight following pregnancy wildfire smoke exposure in more than 1.5 million newborns in Brazil: A nationwide case-control study. *Lancet Reg. Health—Am.* **2022**, 11, 100229.

(33) Zhang, B.; Weuve, J.; Langa, K. M.; D'Souza, J.; Szpiro, A.; Faul, J.; Mendes de Leon, C.; Gao, J.; Kaufman, J. D.; Sheppard, L.; Lee, J.; Kobayashi, L. C.; Hirth, R.; Adar, S. D. Comparison of Particulate Air Pollution From Different Emission Sources and Incident Dementia in the US. *JAMA Internal Medicine* **2023**, 183 (10), 1080–9.

(34) Cleland, S. E.; Wyatt, L. H.; Wei, L.; Paul, N.; Serre, M. L.; West, J. J.; Henderson, S. B.; Rappold, A. G. Short-Term Exposure to Wildfire Smoke and PM_{2.5} and Cognitive Performance in a Brain-Training Game: A Longitudinal Study of U.S. Adults. *Environmental Health Perspectives* **2022**, 130 (6), 067005.

(35) Gao, Y.; Huang, W.; Yu, P.; Xu, R.; Yang, Z.; Gasevic, D.; Ye, T.; Guo, Y.; Li, S. Long-term impacts of non-occupational wildfire exposure on human health: A systematic review. *Environ. Pollut.* **2023**, 320, 121041.

(36) Gao, Y.; Huang, W.; Xu, Z.; Xu, R.; Gasevic, D.; Liu, Y.; Yue, X.; Zhou, G.; Zhang, Y.; Song, J.; Liu, H.; Guo, Y.; Li, S. Wildfire-related PM_{2.5} and cause-specific cancer mortality. *Ecotoxicology and Environmental Safety* **2024**, 285, 117023.

(37) Cao, Y.; Wu, J. Impacts of wildfire smoke PM_{2.5}, greenspace and terrain ruggedness on life expectancy in the contiguous United States. *Science of The Total Environment*. **2025**, 964, 178584.

- (38) Childs, M. L.; Li, J.; Wen, J.; Heft-Neal, S.; Driscoll, A.; Wang, S.; Gould, C. F.; Qiu, M.; Burney, J.; Burke, M. Daily Local-Level Estimates of Ambient Wildfire Smoke PM_{2.5} for the Contiguous US. *Environmental Science & Technology* **2022**, *56* (19), 13607–21.
- (39) Casey, J. A.; Kioumourtoglou, M.-A.; Padula, A.; González, D. J. X.; Elser, H.; Aguilera, R.; Northrop, A. J.; Tartof, S. Y.; Mayeda, E. R.; Braun, D.; Dominici, F.; Eisen, E. A.; Morello-Frosch, R.; Benmarhnia, T. Measuring long-term exposure to wildfire PM_{2.5} in California: Time-varying inequities in environmental burden. *Proceedings of the National Academy of Sciences* **2024**, *121* (8), No. e2306729121.
- (40) Davis, A. C.; Voelkel, J. L.; Remmers, C. L.; Adams, J. L.; McGlynn, E. A. Comparing Kaiser Permanente Members to the General Population: Implications for Generalizability of Research. *Perm. J.* **2023**, *27* (2), 87–98.
- (41) Xiang, A. H.; Wang, X.; Martinez, M. P.; Walthall, J. C.; Curry, E. S.; Page, K.; Buchanan, T. A.; Coleman, K. J.; Getahun, D. Association of Maternal Diabetes With Autism in Offspring. *JAMA* **2015**, *313* (14), 1425–34.
- (42) Coleman, K. J.; Lutsky, M. A.; Yau, V.; Qian, Y.; Pomichowski, M. E.; Crawford, P. M.; Lynch, F. L.; Madden, J. M.; Owen-Smith, A.; Pearson, J. A.; Pearson, K. A.; Rusinak, D.; Quinn, V. P.; Croen, L. A. Validation of Autism Spectrum Disorder Diagnoses in Large Healthcare Systems with Electronic Medical Records. *Journal of Autism and Developmental Disorders* **2015**, *45* (7), 1989–96.
- (43) Jo, H.; Eckel, S. P.; Wang, X.; Chen, J.-C.; Cockburn, M.; Martinez, M. P.; Chow, T.; Molshatzki, N.; Lurmann, F. W.; Funk, W. E.; Xiang, A. H.; McConnell, R. Sex-specific associations of autism spectrum disorder with residential air pollution exposure in a large Southern California pregnancy cohort. *Environ. Pollut.* **2019**, *254*, 113010.
- (44) Xiang, A. H.; Wang, X.; Martinez, M. P.; Page, K.; Buchanan, T. A.; Feldman, R. K. Maternal Type 1 Diabetes and Risk of Autism in Offspring. *JAMA* **2018**, *320* (1), 89–91.
- (45) Heft-Neal, S.; Gould, C. F.; Childs, M. L.; Kiang, M. V.; Nadeau, K. C.; Duggan, M.; Bendavid, E.; Burke, M. Emergency department visits respond nonlinearly to wildfire smoke. *Proceedings of the National Academy of Sciences* **2023**, *120* (39), No. e2302409120.
- (46) Ha, S.; Abatzoglou, J. T.; Adebisi, A.; Ghimire, S.; Martinez, V.; Wang, M.; Basu, R. Impacts of heat and wildfire on preterm birth. *Environmental Research* **2024**, *252*, 119094.
- (47) Stowell, J. D.; Sue Wing, I.; Romitti, Y.; Kinney, P. L.; Wellenius, G. A. Emergency department visits in California associated with wildfire PM_{2.5}: differing risk across individuals and communities. *Environmental Research: Health* **2025**, *3* (1), 015002.
- (48) Ma, Y.; Zang, E.; Liu, Y.; Wei, J.; Lu, Y.; Krumholz, H. M.; Bell, M. L.; Chen, K. Long-term exposure to wildland fire smoke PM_{2.5} and mortality in the contiguous United States. *Proceedings of the National Academy of Sciences* **2024**, *121* (40), No. e2403960121.
- (49) Di, Q.; Amini, H.; Shi, L.; Kloog, I.; Silvern, R.; Kelly, J.; Sabath, M. B.; Choirat, C.; Koutrakis, P.; Lyapustin, A.; Wang, Y.; Mickley, L. J.; Schwartz, J. An ensemble-based model of PM(2.5) concentration across the contiguous United States with high spatiotemporal resolution. *Environ. Int.* **2019**, *130*, 104909.
- (50) Requia, W. J.; Di, Q.; Silvern, R.; Kelly, J. T.; Koutrakis, P.; Mickley, L. J.; Sulprizio, M. P.; Amini, H.; Shi, L.; Schwartz, J. An Ensemble Learning Approach for Estimating High Spatiotemporal Resolution of Ground-Level Ozone in the Contiguous United States. *Environ. Sci. Technol.* **2020**, *54* (18), 11037–47.
- (51) Ritz, B.; Liew, Z.; Yan, Q.; Cuia, X.; Virk, J.; Ketzler, M.; Raaschou-Nielsen, O. Air pollution and autism in Denmark. *Environmental Epidemiology* **2018**, *2* (4), e028.
- (52) Carter, S. A.; Rahman, M. M.; Lin, J. C.; Chow, T.; Yu, X.; Martinez, M. P.; Levitt, P.; Chen, Z.; Chen, J.-C.; Eckel, S. P.; Schwartz, J.; Lurmann, F. W.; Kleeman, M. J.; McConnell, R.; Xiang, A. H. Maternal exposure to aircraft emitted ultrafine particles during pregnancy and likelihood of ASD in children. *Environment International* **2023**, *178*, 108061.
- (53) Carter, S. A.; Rahman, M. M.; Lin, J. C.; Shu, Y. H.; Chow, T.; Yu, X.; Martinez, M. P.; Eckel, S. P.; Chen, J. C.; Chen, Z.; Schwartz, J.; Pavlovic, N.; Lurmann, F. W.; McConnell, R.; Xiang, A. H. In utero exposure to near-roadway air pollution and autism spectrum disorder in children. *Environment International* **2022**, *158*, 106898.
- (54) Bekkar, B.; Pacheco, S.; Basu, R.; DeNicola, N. Association of Air Pollution and Heat Exposure With Preterm Birth, Low Birth Weight, and Stillbirth in the US: A Systematic Review. *JAMA Network Open* **2020**, *3* (6), No. e208243.
- (55) Chang, Y.-S.; Chen, L.-W.; Yu, T.; Lin, S.-H.; Kuo, P.-L. Preterm birth and weight-for-gestational age for risks of autism spectrum disorder and intellectual disability: A nationwide population-based cohort study. *Journal of the Formosan Medical Association* **2023**, *122* (6), 493–504.
- (56) Gardener, H.; Spiegelman, D.; Buka, S. L. Perinatal and Neonatal Risk Factors for Autism: A Comprehensive Meta-analysis. *Pediatrics* **2011**, *128* (2), 344–55.
- (57) R Core Team. R: A language and environment for statistical computing, Ver. 4.1.2; R Foundation for Statistical Computing: Vienna, Austria, 2021.
- (58) Therneau, T. M. A Package for Survival Analysis in R, December 17, 2024.
- (59) Schlegel, R. W.; Smit, A. J. heatwaveR: A central algorithm for the detection of heatwaves and cold-spells. *Journal of Open Source Software* **2018**, *3* (27), 821.
- (60) Burke, M.; Heft-Neal, S.; Li, J.; Driscoll, A.; Baylis, P.; Stigler, M.; Weill, J. A.; Burney, J. A.; Wen, J.; Childs, M. L.; Gould, C. F. Exposures and behavioural responses to wildfire smoke. *Nature Human Behaviour* **2022**, *6* (10), 1351–61.
- (61) Chun, H.; Leung, C.; Wen, S. W.; McDonald, J.; Shin, H. H. Maternal exposure to air pollution and risk of autism in children: A systematic review and meta-analysis. *Environ. Pollut.* **2020**, *256*, 113307.
- (62) Raz, R.; Roberts, A. L.; Lyall, K.; Hart, J. E.; Just, A. C.; Laden, F.; Weisskopf, M. G. Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case-control analysis within the Nurses' Health Study II Cohort. *Environ. Health Perspect.* **2015**, *123* (3), 264–70.
- (63) Volk, H. E.; Lurmann, F.; Penfold, B.; Hertz-Picciotto, I.; McConnell, R. Traffic-related air pollution, particulate matter, and autism. *JAMA Psychiatry* **2013**, *70* (1), 71–7.
- (64) Kostović, I.; Radoš, M.; Kostović-Srzić, M.; Krsnik, Ž. Fundamentals of the Development of Connectivity in the Human Fetal Brain in Late Gestation: From 24 Weeks Gestational Age to Term. *Journal of Neuropathology & Experimental Neurology* **2021**, *80* (5), 393–414.
- (65) Davis, E. P.; Buss, C.; Muftuler, L. T.; Head, K.; Hasso, A.; Wing, D. A.; Hobel, C.; Sandman, C. A. Children's Brain Development Benefits from Longer Gestation. *Front. Psychol.* **2011**, *2*, 1.
- (66) Windham, G. C.; Zhang, L.; Gunier, R.; Croen, L. A.; Grether, J. K. Autism spectrum disorders in relation to distribution of hazardous air pollutants in the san francisco bay area. *Environ. Health Perspect.* **2006**, *114* (9), 1438–44.
- (67) Fang, T.; Guo, H.; Zeng, L.; Verma, V.; Nenes, A.; Weber, R. J. Highly Acidic Ambient Particles, Soluble Metals, and Oxidative Potential: A Link between Sulfate and Aerosol Toxicity. *Environ. Sci. Technol.* **2017**, *51* (5), 2611–20.
- (68) Verma, V.; Polidori, A.; Schauer, J. J.; Shafer, M. M.; Cassee, F. R.; Sioutas, C. Physicochemical and Toxicological Profiles of Particulate Matter in Los Angeles during the October 2007 Southern California Wildfires. *Environmental Science & Technology* **2009**, *43* (3), 954–60.
- (69) Silveira, S.; Kornbluh, M.; Withers, M. C.; Grennan, G.; Ramanathan, V.; Mishra, J. Chronic Mental Health Sequelae of Climate Change Extremes: A Case Study of the Deadliest Californian Wildfire. *International Journal of Environmental Research and Public Health* **2021**, *18* (4), 1487.

(70) Rodney, R. M.; Swaminathan, A.; Caele, A. L.; Christensen, B. K.; Lal, A.; Lane, J.; Leviston, Z.; Reynolds, J.; Trevenar, S.; Vardoulakis, S.; Walker, I. Physical and Mental Health Effects of Bushfire and Smoke in the Australian Capital Territory 2019–20. *Frontiers in Public Health* **2021**, *9*, 682402.

(71) To, P.; Eboreime, E.; Agyapong, V. I. O. The Impact of Wildfires on Mental Health: A Scoping Review. *Behavioral Sciences* **2021**, *11* (9), 126.

(72) Mirabelli, M. C.; Vaidyanathan, A.; Pennington, A. F.; Ye, D.; Trenga, C. A. Wildfire smoke and symptoms affecting mental health among adults in the U.S. *State of Oregon. Preventive Medicine* **2022**, *164*, 107333.

(73) Manzari, N.; Matvienko-Sikar, K.; Baldoni, F.; O’Keeffe, G. W.; Khashan, A. S. Prenatal maternal stress and risk of neurodevelopmental disorders in the offspring: a systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology* **2019**, *54* (11), 1299–309.

The advertisement features a vertical image on the left showing a blue, translucent, spherical object with a textured surface, connected by a yellow, rope-like structure to a green and pink, textured, spherical object. The background is a solid dark blue. Text is overlaid on the right side in white and yellow.

CAS BIOFINDER DISCOVERY PLATFORM™

**PRECISION DATA
FOR FASTER
DRUG
DISCOVERY**

CAS BioFinder helps you identify
targets, biomarkers, and pathways

Unlock insights

CAS
A division of the
American Chemical Society