# Researchers link early-life exposure to wildfire smoke with early use of upper respiratory medication

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Spatial distribution of total number of wildfire smoke-days (2010–2016) at each MSA for the (a) 0%, b 25%, and (c) 50% thresholds. Thresholds are defined as the population-weighted percentage of zip codes within a Metropolitan Statistical Area (MSA) required to experience a smoke-day, in order to assign a smoke-day to the MSA

Children exposed to wildfire smoke in the first trimester of pregnancy or the first few weeks after birth are more likely to be prescribed upper

respiratory medication earlier in life, according to a new study from researchers at UNC-Chapel Hill and the United States Environmental Protection Agency (EPA).

Wildfires are one of the largest sources of air pollution and have a significant impact on respiratory health. In the U.S., they have been growing in frequency and severity over the past two decades due to things like climate change and population growth, particularly in western states. Smoke from these fires carries a hazardous mixture of chemical compounds, particulate matter (PM) and fine particulate matter (PM2.5) that contribute to poor health—including exacerbation of asthma and reduced lung function in children.

While research has shed light on many of the health effects that come from PM in wildfire smoke, experts are still trying to understand how wildfire PM might affect children in their earliest stages of development. The UNC-led study, published recently in *Environmental Health*, sought to investigate whether exposure to wildfire smoke in-utero or in the first weeks of life resulted in earlier usage of medications to treat respiratory conditions.

These medications can include cetirizine (Zyrtec) and mometasone for upper respiratory treatment, albuterol for lower respiratory treatment, and methylprednisolone, prednisolone or prednisone for systemic anti-inflammatory treatment.

Results from the study suggest that infants who are exposed to wildfire smoke during the first trimester or the first six months of life may be at greater risk of upper respiratory illness in early childhood, according to Radhika Dhingra, Ph.D., adjunct assistant professor of environmental sciences and engineering at the UNC Gillings School of Global Public Health and medical student at the Brody School of Medicine at East Carolina University, who is first author on the study.

Dhingra collaborated on the study with several EPA and UNC colleagues, including Ilona Jaspers, Ph.D., professor of pediatrics, microbiology and immunology at the UNC School of Medicine, environmental sciences and engineering at the Gillings School, and director of the UNC Center for Environmental Medicine, Asthma and Lung Biology (CEMALB); and Ana G. Rappold, Ph.D., Branch Chief of the Clinical Research branch, statistician at EPA and adjunct associate professor of environmental sciences and engineering at the Gillings School.

Using data from private insurance claims in an IBM MarketScan database, the study team linked a group of 182,387 live births in Oregon, California, Montana, Nevada and Idaho to wildfire smoke exposure estimates based on Hazard Mapping System Fire and Smoke Product data, which is compiled by the U.S. National Oceanic and Atmospheric Administration. They measured smoke exposure during each trimester and two postnatal periods (0-12 weeks and 13–24 weeks), as well as the time it took to first fill an upper respiratory, lower respiratory or anti-inflammatory prescription, if a child needed one.

The team used these data to produce a statistical measurement called a hazard ratio, which estimated the association between the average weekly smoke exposure days and the time to first prescription fill for each developmental period. Hazard ratios greater than one suggested that a child exposed to wildfire smoke during a given period used a respiratory medication sooner than children who had no exposure to wildfire smoke during that same period.

In addition to finding that first trimester and post-birth exposure to wildfire smoke shortened the time to the first use of upper respiratory medication, researchers found that in utero exposure to wildfire smoke resulted in an increase in time until the first use of lower-respiratory and anti-inflammatory medications.

The reason for this unexpected inverse relationship was unclear. Researchers noted that one explanation could be a live birth bias, which often happens in perinatal epidemiological studies because data are limited to live births and cannot include information on pregnancy loss. It could also be a sign of a biological process in reaction to smoke exposure in utero.

Additionally, the team observed biological sex-linked differences in the results. The time to first use of upper respiratory medication was shorter in female children exposed to wildfire smoke the first trimester and the first 12-week postnatal period, while it was shorter for male children in the 13–24 postnatal week period. According to the study, these results are consistent with other findings that suggest sex differences in lung development and wildfire smoke vulnerability.

Jaspers suggested that the difference between upper and lower respiratory results could be related to the difference in the way children were exposed to wildfire smoke. "The effects measured in the upper respiratory tract were likely caused by infants directly inhaling wildfire smoke via the nasal cavity," she explained, "while the first trimester effects were indirect via the mother's exposure. Infants are obligate nose-breathers and would potentially have significant nasal exposure during wildfire episodes."

The upper and lower respiratory tracts are also structurally and functionally different, which researchers say may have an impact on the effects the study measured.

"The upper respiratory tract comprises the nasal cavity, larynx and pharynx, while the lower respiratory tract is the bronchi and lungs," Dhingra explained. "The structure, immune protection mechanisms, and even the microbiome vary between the two. This variation in physiological and immunological functions may explain why these two

portions of the respiratory tract do not behave the same way in response to wildfire smoke."

To further explore the complexity of these findings, Dhingra and fellow co-author Meghan Rebuli, Ph.D., assistant professor of pediatrics at the School of Medicine and at CEMALB, are currently researching how the microbiome and immune system interact in the nose (part of the upper respiratory tract) and sputum (a substance produced by the lower respiratory tract) as a result of wildfire smoke exposure in adults.

"With this work, we hope to shed some light on the complex relationship between the upper and lower respiratory tracts," she said.

**More information:** Radhika Dhingra et al, Wildfire smoke exposure and early childhood respiratory health: a study of prescription claims data, *Environmental Health* (2023). DOI: 10.1186/s12940-023-00998-5

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