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The Impact of Prescribed Fire versus Wildfire on the Immune and Cardiovascular Systems of Children

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To the Editor:

The increase in wildfires associated with climate change augments the impact of air pollution on health in many areas of the country. When wildfires occur, there is an increase in asthma attacks and associated co-morbidities,^{1,2} especially for asthma hospitalization in ages 0 to 5 years³ and more recently it has been shown that there are increases in cardiovascular events⁴. Given the health risks associated with high intensity wildfires, there is motivation to increase the use of lower intensity prescribed fires. Prescribed burns decrease the build-up of flammable vegetation and subsequent fuel for wildfires, mitigating the spread and intensity of wildfires. However, prescribed fire raises public concerns because of the additional pollutant exposure.

Therefore, our objective is to determine whether there are differential health consequences with a prescribed fire vs wildfire. We focus on children given their reduced lung size, increased metabolic rates, higher respiratory rate and developing immune systems⁵, and because in macaque monkeys who are exposed to wildfire smoke in infancy, there is associated immune dysregulation and decreased lung function in adolescence⁶. We hypothesize that the health impacts of a prescribed fire are less detrimental to the respiratory and cardiovascular systems than a wildfire in school-aged children and that T cell skewing and epigenetic modulation will occur with exposure to wildfire more than from exposure to a prescribed fire.

We analyzed data collected from a convenience sample of subjects (n=220) over a period of 2 years living in Fresno, CA, all of whom were potentially exposed to smoke from fires, which consisted of similar varieties of coniferous trees, in nearby Yosemite National Park. Health questionnaires, blood samples, and vital signs were collected and subjects were selected that had their blood drawn 3 months after a prescribed burn or wildfire, because our prior research indicates that this time frame is associated with increased methylation of the Foxp3 gene⁷. Using this criteria, we analyzed data from 32 children (median age=7 [range 7;8]yrs, 38% asthmatic as per NHLBI guidelines) exposed to a prescribed burn 70 miles away covering 553 acres in March, 2015, and 36 children (median age=8 [range 7;8]yrs,

25% asthmatic) exposed to a wildfire 70 miles away covering 415 acres in September, 2015. A control group of 18 children was also compared (median age=8 [range 7,8]yrs; 21% asthmatic), who had no obvious exposure to wildfires or prescribed burns and were living in the San Francisco Bay area, where pollution levels are consistently low (i.e. less than 10 $\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$). All subjects were consented with an IRB-approved protocol.

Pollution exposure was measured from 4 central site monitors and both distance-weighted to the subject's home as in previous studies⁸ and averaged across the monitoring sites. Peripheral blood mononuclear cells were stained with metal-conjugated antibodies for surface markers and CyTOF was performed. Methylation studies using pyrosequencing were performed per published methods⁶ on selected CpG sites of the *Foxp3*, *IL-4*, *IL-10* and *IFN γ* genes.

As shown in Figure 1, all pollutant levels were higher in the wildfire group (n=36) than the prescribed burn (n=32) groups ($p<.0001$; wildfire vs prescribed means: $\text{NO}_2=10.7$ ppb ± 0.3 vs 4.0 ppb ± 0.2 ; $\text{NO}_x=25.6$ ppb ± 1.0 vs 9.9 ppb ± 0.5 ; $\text{PAH}_{456}=11.4$ ng/ m^3 ± 0.4 vs 5.3 ng/ m^3 ± 0.2 ; $\text{EC}=1.0$ $\mu\text{g}/\text{m}^3$ ± 0.02 vs 0.48 $\mu\text{g}/\text{m}^3$ ± 0.01 ; $\text{CO}=0.56$ ppm ± 0.02 vs .25 ppm ± 0.01 ; $\text{PM}_{10}=41.5$ $\mu\text{g}/\text{m}^3$ ± 1.1 vs 28.0 $\mu\text{g}/\text{m}^3$ ± 0.3 ; $\text{PM}_{2.5}=15.9$ $\mu\text{g}/\text{m}^3$ ± 0.4 vs 10.0 $\mu\text{g}/\text{m}^3$ ± 0.2). In addition, average $\text{PM}_{2.5}$ levels were calculated 2 weeks prior to each fire, throughout each fire and 2 weeks after each fire to determine the potential contributions of each fire. $\text{PM}_{2.5}$ levels increased during the wildfire and then returned to baseline indicating that the wildfire was likely associated with the rise in $\text{PM}_{2.5}$ levels (2 weeks prior mean=9.3 $\mu\text{g}/\text{m}^3$ [SD=2.5]; during fire mean=13.7 $\mu\text{g}/\text{m}^3$ [SD=5.7] vs 2 weeks after mean=9.1 $\mu\text{g}/\text{m}^3$ [SD=1.9]). For the prescribed fire, the $\text{PM}_{2.5}$ levels decreased 12 $\mu\text{g}/\text{m}^3$ from pre to post fire, indicating that the prescribed burn likely did not contribute substantially to $\text{PM}_{2.5}$ levels (2 weeks prior mean=17.8 $\mu\text{g}/\text{m}^3$ [SD=5.9]; duration of fire mean=8.5 $\mu\text{g}/\text{m}^3$ [SD=3.5]; 2 weeks post mean=5.8 $\mu\text{g}/\text{m}^3$ [SD=2.4]).

To investigate the immune system, immunophenotype results were compared with a one-way ANOVA across the 3 groups for percent Th1 cells (CD4+, CXCR3+, CCR5+), revealing significant differences among groups ($p<.0001$) as shown in Figure 2, with the lowest Th1% for the wildfire group (control 5.19% ± 1.89 ; prescribed fire 3.99% ± 0.34 ; wildfire 2.04% ± 0.31). There were no significant differences between the groups for other immune cell types such as Th2 cells (CD4+, CCR4+, CCR6-; $p=0.14$) or T regulatory cells (CD4+, CD 25+, CD 127-; $p=0.66$).

Methylation levels between the prescribed and wildfire groups were compared using linear regression models while controlling for covariates (age, sex, BMI percentile, race, second-hand smoke and asthma status). *Foxp3* methylation in the promoter region of DNA isolated from the same blood samples was increased post wildfire exposure compared to prescribed fire exposure (B estimate (est)=2.59; Standard Error (SE)=0.95; $p=0.01$). Moreover, there was a trend toward worsened health outcomes in the wildfire group compared to the prescribed group, including increases in wheezing episodes in those with no prior history of asthma, increases in asthma exacerbations in those with prior asthma, and rises in pulse pressure (est=4.08; SE=2.35; $p=0.09$).

The increase in Foxp3 methylation associated with the wildfire is consistent with prior air pollution studies^{7,8}. The reduction in Th1 pro-inflammatory T cells associated with wildfire exposure may be consistent with the molecular heterogeneity of asthma and associated endotypes⁹. Moreover, in cardiovascular disease, which is an inflammatory process and also associated with air pollution and wildfires, Th1 cells have been associated with immunity in atherosclerosis¹⁰. While this is a descriptive, retrospective study and the PM levels do not distinguish from various sources including fires, these preliminary results suggest future studies are needed. This will allow us to both understand the mechanism by which wildfire exposure impacts the immune system and to investigate the health impact of prescribed fire versus wildfire, as there is heightened motivation to increase the application of prescribed burns to combat the risks of increasing wildfire size and intensity in several areas of the country.

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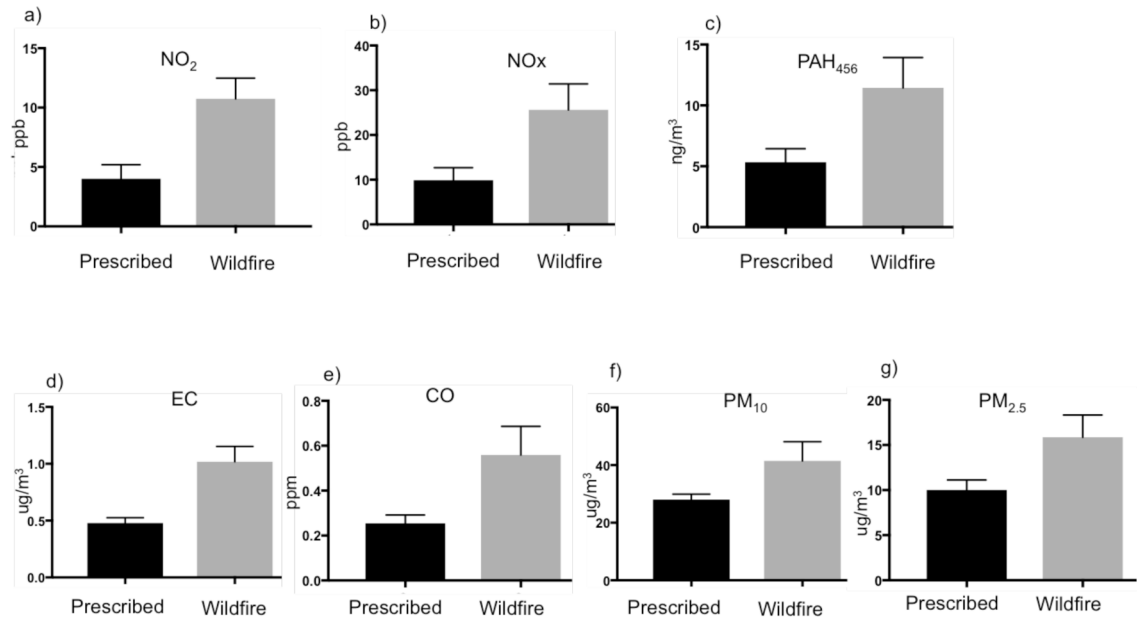


Figure 1: Average levels of pollutants during the wildfire and prescribed fire. When comparing prescribed vs wildfire, $p < .0001$ for each pollutant shown.

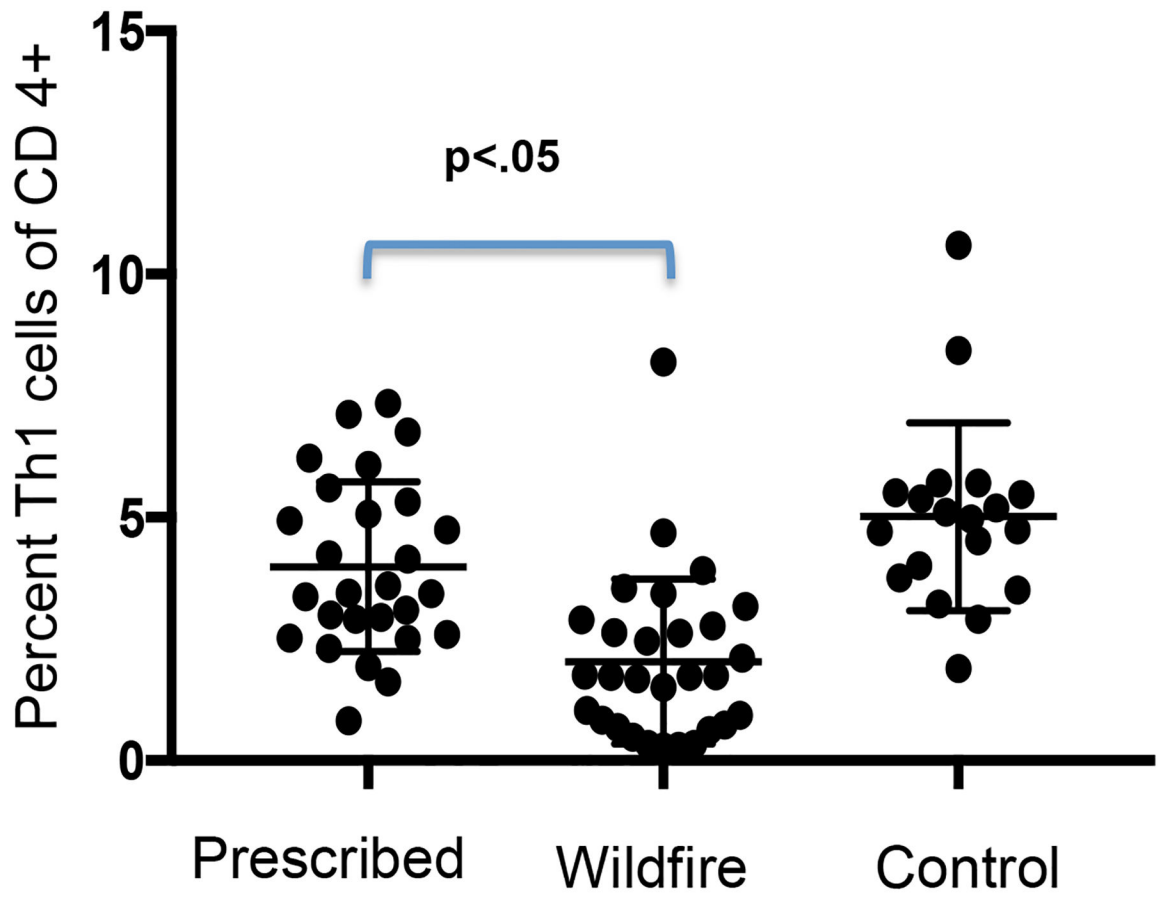


Figure 2:
Th1 Cell percentage of CD 4+ cells for children 90 days after being exposed to a prescribed fire, wildfire or no exposure (1-way ANOVA, $p < .0001$).