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LETTER TO THE EDITOR

WILEY

Reduction in forced vital capacity in asthmatic children on days with bushfire smoke exposure in the Australian 2019/2020 bushfire

While bushfires have long been a part of Australia's ecosystem, the 2019–20 bushfires were an unprecedented event leading to 5.5 million hectares of land being affected in New South Wales (NSW) alone.[1] This is approximately the same as the area burnt in the combined bushfire seasons of 1993–94 and 2018–19.[2] Air pollution has been recognized as a risk factor for asthma development.[3] An increase in emergency department visits and hospital admissions has been described in asthmatic children exposed to bushfire smoke.[4] Bushfire smoke contains a complex range of gases and particles, including a particulate matter measuring less than 2.5 microns ($PM_{2.5}$) composition, carbon monoxide, ozone, methane, and nitrogen oxides which is different from the one emitted by fossil fuel combustion.[5] The NSW Air Quality Monitoring Network reported that 74% of the spring and summer days in 2019–20 met poor air quality standards according to the Air Quality Index.[6] This study therefore aimed to determine the effects of bushfire smoke exposure during the 2019–20 bushfire season on lung function in asthmatic children.

Our study used routinely collected data from children with asthma who attended the John Hunter Children's Hospital outpatient childhood asthma clinic between January 2019 and April 2020. Data were collected from electronic medical records and clinical lung function databases from children aged 4 to 16 years of age, with a confirmed diagnosis of asthma seen by a Pediatric respiratory specialist. Only children with a valid spirometry meeting ATS/ERS standards during their clinical visit were included.[7] Before the appointment, parents and patients were instructed not to take the following medications for the times indicated, unless they are breathless and need to use them: short-acting inhalers (Ventolin, Atrovent, Flixotide, Bricanyl, Asmol, Airomir, Epaq) for 8 h; and long-acting inhalers (Symbicort, Seretide, Serevent, Spiriva, Oxis, Foradile) for 12 h. Data included demographic characteristics, lung function (spirometry and fraction of exhaled nitric oxide at a flow rate of 50 ml/s [FeNO50] if available), and symptom control in the past 4 weeks. Global Lung Initiative (GLI) reference equations were used to calculate spirometry measurements (FEV1, FVC, and FEV1/FVC ratio percent of predicted value [% predicted]). Bronchodilator reversibility was calculated after administration of inhaled rapid-onset beta2 agonist bronchodilator (SABA).[8] For first nation Australian children, the GLI 'Other/Mixed equation reference' was used for the data collection.

$PM_{2.5}$ exposure during the period was assessed for participants located within the Sydney Greater Metropolitan Region (GMR) study region in NSW, an area of approximately 1860 square kilometers. Daily 24-h mean $PM_{2.5}$ data from fixed-site government air quality monitoring stations within the study regions were measured[9] and interpolated using an inverse distance weighting procedure to estimate daily $PM_{2.5}$ exposure concentration for participant's residential location.[10]

Bushfire days were defined when three prerequisites were met: (1) the entire study region's 24-h average of $PM_{2.5}$ concentration exceeded the 95th percentile (based on the period 01/01/2010 to 31/12/2018 for the Sydney GMR), (2) visual confirmation of fire for that day or up to 3 days before or after via satellite imagery, and (3) interpolated $PM_{2.5}$ reading for each participant's residential address also exceed the 95th percentile for the region, to control for spatial variability in the region.[10] This approach has been successfully used to identify bushfire-smoke-affected study days in several previous epidemiological studies.[10,11]

Categorical measures were described using counts and percentages, while continuous measures were characterized using means with standard deviation (SD). Statistical significances were calculated using two-tailed Mann–Whitney U test or Student's *t* test as appropriate and chi-square test if categorical. As this was a longitudinal study with different time points, we used mixed effect regression models with a random intercept to estimate the total effect of bushfire-related smoke exposure on lung function of children. Outputs of fixed and random effects were calculated for the presence of bushfire smoke on the day of the test and for $PM_{2.5}$ levels on the day of the lung function testing. Models were adjusted to account for differences found between the groups in the univariate analysis and to account for factors that usually can influence lung function, including sex, age, weight, height, being a first nation Australian, tobacco smoke exposure at home, and season. A specific sample size was not targeted; instead, a convenience sample was used. Statistical analysis was performed using STATA version 15 (Texas, USA). A *p*-value of $<.05$ was considered statistically significant. This study was approved by the Hunter

New England Human Research Ethics Committee (2020/ETH00361). As we collected data from medical records and clinical databases, a waiver of consent was granted. One hundred twenty-nine children visited the asthma clinic and performed lung function tests. Of those, 49 children attended one visit, 78 children attended two visits, one child attended three visits, and one child attended four visits, leaving us with a sample of 212 occasions. $PM_{2.5}$ levels and bushfire information were available for all visits. We compared data collected on a non-bushfire day ($n = 176$) to those on a bushfire day ($n = 36$). Groups were similar within themselves. Of note, first nation Australian children were more likely to be tested on a bushfire day (19.4% vs 5.8%, $p = .01$) and were found to reside in rural areas more commonly in this study; however, first nation Australian children did not differ on lung function values compared to non-first nation Australian children ($p = .642$). No differences were found in the Asthma Control Test (ACT) score for children tested on a bushfire day and children tested on a non-bushfire day.

As expected $PM_{2.5}$ mean levels at visit day were significantly higher on a bushfire day (35.7 μg/m^3 [SD = 16.8, Min = 15.0, Max = 71.6] vs 8.3 μg/m^3 [SD = 3.2, min = 3.3, max = 20.8], $p < .001$). Using mixed model a significant mean decrease of 5% in FVC% predicted was found in asthmatic children when they visited the clinic on a bushfire day (Table 1). Notably, the FVC decline was ameliorated 10 min after administration of bronchodilators (−3.00, 95% CI −6.83 to 0.82, $p = .12$). No significant decrease was found in FEV_1 and FEV1/FVC ratio % predicted. When taking data from same children tested both on a bushfire and non-bushfire ($n = 59$), the effects of a bushfire day were comparable, even though the significance levels were not reached (−4.36, 95% CI −9.24 to 0.55, $p = .08$). When analyzing mean $PM_{2.5}$ concentrations on the day of the clinic visit as a continuous independent variable, we found a significant decrease in FVC and FEV% predicted for each μg per cubic meter increase in $PM_{2.5}$ (Table 1).

Our results show for the first time that wildfire exposure around the time of lung function testing is associated with a mean decrease of 5% in FVC % predicted in asthmatic children. This effect size is considered to be of clinical importance.[5,12,13] For instance, specific cystic fibrosis (CF) transmembrane conductance regulator (CFTR) modulators have demonstrated a therapeutical effect improvement of around 5% in FEV1 and FVC and their use in CF patients is nowadays accepted standard of care.[14] We observed that the FVC decline may be, at least in part, reversible after bronchodilator inhalation. The improvement in FVC—which is static volumes of the lung—after SABA administration might be due to the reduction in the child's hyperinflation, improving inspiratory capacity. In adults with Chronic Obstructive Pulmonary Disease (COPD), administration of bronchodilator results in less air trapping as it allows better lung emptying, reducing the work of breathing.[15] It has been suggested that in adults with severe airway obstruction changes in FVC should be evaluated as a clinically important relief of hyperinflation.[16] In children, this needs further investigation to verify the clinical importance of a reduction in FVC.

TABLE 1 Effect of bushfire exposure and according to bushfire-related smoke exposure on lung function of asthmatic children

Demographics	Data collected on a bushfire day ($n = 36$)			Data collected on a non-bushfire day ($n = 176$)		*p*-value
Male % (n)	66.7% (24)			52.8% (93)		.14
First Nation Australian % (n)	19.4% (4)			5.8% (10)		.01
Age Mean (SD)	10.6 (3.3)			10.6 (3.6)		.93
Weight Mean (SD)	44.6 (25.1)			39.3 (16.9)		.12
Height Mean (SD)	143.4 (20.5)			141 (19.7)		.51
Smoking exposure % (n)	27.8% (10/36)			16.7% (29/174)		.16
Beclomethasone dosage ($n = 130$) Mean (SD)	659.1 (436.1)			689.4 (458.4)		.78
Asthma Control Score Median (IQR)	21 (17–24)			20 (16–23)		.80
PM 2.5 day Mean (SD)	35.7 (16.8)			8.3 (3.2)		<.001
Mixed model	Clinic visit on a bushfire day Adjusted			Mean PM2.5 on the clinic visit day Adjusted		
	β	95% CI	*p*	β	95% CI	*p*
FVC % pred ($n = 207$)	−4.75	−8.98; −0.51	.028	−0.19	−0.301; −0.048	.002
FEV_1 % pred ($n = 207$)	−1.69	−6.19; 2.81	.462	−0.14	−0.265; −0.005	.041
FEV1/FVC ratio % pred ($n = 207$)	1.21	−1.62; 4.03	.402	0.00	−0.09; 0.08	.938
FeNO ppb ($n = 174$)	−3.73	−9.56; 2.09	.209	−0.15	−0.32; 0.02	.077
ACT ($n = 153$)	0.73	−1.02; 2.48	.416	0.03	−0.03; 0.08	.312

Note: For baseline characteristics, parameters are presented as mean (SD), linear mixed effect models adjusted for sex, age, weight, height, first nation Australian status, and smoking exposure. Beta coefficient for PM2.5 results is shown for each μg per cubic meter increase in $PM_{2.5}$.

Our modeling suggests that exposure to the highest mean $PM_{2.5}$ concentration of 71.6 μg/m^3 on bushfire days in this study may result in a decrease of 14% in FVC % predicted and 10% in FEV_1 % predicted compared to the lower level of 8.3 μg/m^3 on non-bushfire days. Smoke exposure to the Australian 2019/2020 bushfire has been linked with adverse effects among both people with and without respiratory conditions in a cross-sectional study using a symptom online survey.[17] To our knowledge, our study is the first to demonstrate the effects of the Australian 2019/2020 using an objective measurement—spirometry—in asthmatic children, as most studies focus on emergency department visits and hospital admissions.[4,18] A recent study in a North American pediatric asthma population only found an association between wildfire smoke exposure and FEV_1 in children older than 12 years of age.[19] A reduction in peak expiratory flow rate was associated with $PM_{2.5}$ wildfire exposure in Brazilian children—however, a greater effect was found in children without asthma than on asthmatic children.[20] While our study result is in line with previous reports, we cannot exclude that the true effect on FEV_1 is so small that it remained undetected as a result of analyzing only a small sample with potentially large variability. In either case, our results suggest that bushfire smoke exposure may predominately result in a restrictive lung function limitation[21] while $PM_{2.5}$ exposure is associated with a mixed, restrictive and obstructive, deficit in asthmatic children. Lung volume studies would be required to confirm this hypothesis. A previous study has shown greater effects of ambient ozone exposure on FVC in a non-selected child cohort from Southern Germany[22] corroborating the hypothesis that a large number of pollutants found in wildfire smoke, including PM and ozone, contribute to the induction of clinically significant FVC deficits. The investigation of potential long-term effects on FVC growth as a result of repeated exposure to bushfire requires further studies.

Differences between $PM_{2.5}$ and PM_{10} effects have been demonstrated. Even though $PM_{2.5}$ is a large fraction of PM_{10}, $PM_{2.5}$ seems to be of greater health concern due to its longer residence time in the atmosphere, and its accumulation due to persistent atmospheric stability which in turn reduces its removal. This may be relevant if we compare our results that investigated $PM_{2.5}$ levels and find a reduction in lung function of asthmatic children with the study by Jalaludin and associates, which did not find an association between levels of PM_{10} during the 1994 Australian bushfire and lung function in children with wheeze.[23] We therefore speculate that finer particulate matter may affect asthmatic children more significantly due to its composition and accumulation in the air. As compared to the study by Jalaludin et al, we also used a satellite confirmation of bushfire, which could be an improved modeling of lung health effects beyond the consideration of particle size.

The strengths of this study include its retrospective longitudinal design, using data from children whose asthma diagnosis is established, whose treatment is supervised by a specialist, and who were measured with identical equipment by clinical staff at a respiratory clinic. Importantly, the lung function effects occurred despite the children receiving specialist asthma treatment. In addition, our data do not suggest a selection bias where children would have attended multiple appointments due to a bushfire episodes as repeated clinical visits were not associated with bushfire days (75% vs 77.3%, $p = .83$) and visits were scheduled as routine follow-ups and not arranged for acute symptoms that arose from bushfire exposure. We used complex and previously employed methodology to classify bushfire day. Limitations of this study include a small and selected sample which might reflect more severe asthma phenotypes, and thus, our results may not be representative for a non-selected pediatric asthma population.

Mechanistically, the toxic effects of bushfire smoke have been linked to oxidative stress[24] and inflammatory responses[25] highlighting potential preventive and therapeutic strategies to reduce lung function deficits and resultant disease burden caused by wildfire smoke exposure, in particular in susceptible populations such as asthmatics.

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REFERENCES

1. NSW Department of Planning. *Hourly Site Average Pollutant Concentration Data for 1994–2018*. NSW Department of Planning; 2019.
2. NSW Department of Planning. Industry and Environment New South Wales Air Quality Monitoring Network.
3. Murphy VE, Karmaus W, Mattes J, et al. Exposure to stress and air pollution from bushfires during pregnancy: could epigenetic changes explain effects on the offspring? *Int J Environ Res Public Health*. 2021;18(14):7465.
4. Mirabelli MC, Künzli N, Avol E, et al. Respiratory symptoms following wildfire smoke exposure: airway size as a susceptibility factor. *Epidemiology*. 2009;20(3):451-459.
5. Cazzola M, MacNee W, Martinez FJ, et al. Outcomes for COPD pharmacological trials: from lung function to biomarkers. *Eur Respir J*. 2008;31(2):416-469.
6. Keywood MD, Hibberd MF, Emmerson KM. Ambient air quality: air quality index. *Australia State of the Environment 2016, Australian Government Department of the Environment and Energy*; 2016.
7. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med*. 2019;200(8):e70-e88.
8. Australia National Asthma Council. *Australian Asthma Handbook—Quick Reference Guide*. National Asthma Council; 2014.
9. Matthew R, John K, Ningbo J, Glenn R, Yvonne S. Air quality monitoring in NSW: from long term trend monitoring to integrated urban services. *Air Quality and Climate Change*. 2020;54(1):44-51.
10. Johnston FH, Hanigan IC, Henderson SB, et al. Creating an integrated historical record of extreme particulate air pollution events in Australian cities from 1994 to 2007. *J Air Waste Manag Assoc*. 2011;61(4):390-398.
11. Morgan G, Sheppeard V, Khalaj B, et al. Effects of bushfire smoke on daily mortality and hospital admissions in Sydney, Australia. *Epidemiology*. 2010;21(1):47-55.
12. du Bois RM, Weycker D, Albera C, et al. Ascertainment of individual risk of mortality for patients with idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2011;184(4):459-466.
13. Zappala CJ, Latsi PI, Nicholson AG, et al. Marginal decline in forced vital capacity is associated with a poor outcome in idiopathic pulmonary fibrosis. *Eur Respir J*. 2010;35(4):830-836.
14. Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor–ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. *N Engl J Med*. 2015;373(3):220-231.
15. Tashkin DP, Celli B, Decramer M, et al. Bronchodilator responsiveness in patients with COPD. *Eur Respir J*. 2008;31(4):742-750.
16. Quanjer PH, Ruppel GL, Langhammer A, et al. Bronchodilator response in FVC is larger and more relevant than in FEV(1) in severe airflow obstruction. *Chest*. 2017;151(5):1088-1098.
17. MacIntyre CR, Nguyen P-Y, Trent M, et al. Adverse health effects in people with and without preexisting respiratory conditions during bushfire smoke exposure in the 2019/2020 Australian summer. *Am J Respir Crit Care Med*. 2021;204(3):368-371.
18. Bui D, Davis S, Flynn A, Bell R, Dharmage S. Impact of recent catastrophic bushfires on people with asthma in Australia: health, social and financial burdens. *Respirology*. 2021;26(4):296-297.
19. Lipner EM, O'Dell K, Brey SJ, et al. The associations between clinical respiratory outcomes and ambient wildfire smoke exposure among pediatric asthma patients at National Jewish Health, 2012–2015. *Geohealth*. 2019;3(6):146-159.
20. Jacobson LDSV, Hacon SDS, Castro HAD, et al. Acute effects of particulate matter and black carbon from seasonal fires on peak expiratory flow of schoolchildren in the Brazilian Amazon. *PLoS One*. 2014;9(8):e104177.
21. Jat KR. Spirometry in children. *Prim Care Respir J*. 2013;22(2):221-229.
22. Ihorst G, Frischer T, Horak F, et al. Long- and medium-term ozone effects on lung growth including a broad spectrum of exposure. *Eur Respir J*. 2004;23(2):292-299.
23. Jalaludin B, Smith M, O'Toole B, Leeder S. Acute effects of bushfires on peak expiratory flow rates in children with wheeze: a time series analysis. *Aust N Z J Public Health*. 2000;24(2):174-177.
24. Wegesser TC, Pinkerton KE, Last JA. California wildfires of 2008: coarse and fine particulate matter toxicity. *Environ Health Perspect*. 2009;117(6):893-897.
25. Franzi LM, Bratt JM, Williams KM, Last JA. Why is particulate matter produced by wildfires toxic to lung macrophages? *Toxicol Appl Pharmacol*. 2011;257(2):182-188.