ANESTHESIOLOGY

Wildfire Smoke Exposure Is Associated with Adverse Respiratory Events under General Anesthesia in At-risk Pediatric Patients

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Worldwide, there is increasing exposure to poor air quality due to wildfires
- Poor air quality has an impact on asthma exacerbations, emergency department visits, and hospitalizations in both adult and pediatric patients

What This Article Tells Us That Is New

- Pediatric patients predisposed to respiratory complications are at increased risk for adverse respiratory events under anesthesia during periods of poor air quality due to wildfire smoke

ABSTRACT

Background: Increasing wildfire activity worldwide has led to exposure to poor air quality and numerous detrimental health impacts. This study hypothesized an association between exposure to poor air quality from wildfire smoke and adverse respiratory events under general anesthesia in pediatric patients.

Methods: This was a single-center retrospective double-cohort study examining two significant wildfire events in Northern California. Pediatric patients presenting for elective surgery during periods of unhealthy air quality were compared with those during periods of healthy air quality. The primary exposure, unhealthy air, was determined using local air quality sensors. The primary outcome was the occurrence of an adverse respiratory event under anesthesia. Secondary analysis included association with other known risk factors for adverse respiratory events.

Results: A total of 625 patients were included in the analysis. The overall risk of a respiratory complication was 42.4% (265 of 625). In children without a history of reactive airway disease, the risk of adverse respiratory events did not change during unhealthy air periods (102 of 253, 40.3%) compared with healthy air periods (95 of 226, 42.0%; relative risk 0.96 [0.77 to 1.19], $P = 0.703$). In children with a history of reactive airway disease, the risk of adverse respiratory events increased from 36.8% (25 of 68) during healthy air periods to 55.1% (43 of 78) during periods with unhealthy air (1.50 [1.04 to 2.17], $P = 0.032$). The effect of air quality on adverse respiratory events was significantly modified by reactive airways disease status (1.56 [1.02 to 2.40], $P = 0.041$).

Conclusions: Pediatric patients with underlying risk factors for respiratory complications under general anesthesia had a greater incidence of adverse respiratory events during periods of unhealthy air quality caused by wildfire smoke. In this vulnerable patient population, postponing elective anesthetics should be considered when air quality is poor.

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Wildfire activity has increased significantly over the past three decades worldwide.[1–4] In 2020, 41 major wildfire events occurred in the United States and Canada,[5] with more than 10 million acres of land burned.[6] An expanding urban–wildland interface,[7] as well as climate change[8] with warmer temperatures, earlier snowmelts, and less rainfall, have likely impacted both the severity and the frequency of fires in the western United States.[9,10]

This article is featured in "This Month in Anesthesiology," page A1. This article is accompanied by an editorial on p. 524. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has an audio podcast. This article has a visual abstract available in the online version. Part of the work presented in this article has been presented as a poster at the Society for Pediatric Anesthesia, Impact of Smoke Exposure from the 2020 Northern California Wildfires on Pediatric Perioperative Adverse Respiratory Events, Virtual Meeting, February 27, 2021; as a poster the International Anesthesia Research Society. Impact of Smoke Exposure from the Northern California Wildfires on Pediatric Perioperative Adverse Respiratory Events. Virtual Meeting, May 15, 2021; and as an oral presentation and a featured abstract poster for the American Society of Anesthesiologists. Impact of Smoke Exposure from the Northern California Wildfires on Pediatric Perioperative Adverse Respiratory Events, San Diego, California, October 9, 2021.

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Wildfire smoke causes air pollution and severely impacts both the environment and human health. Smoke contains many detrimental compounds, including the gaseous compounds ozone, carbon monoxide, and nitrous and sulfur-containing oxides, as well as particulate matter. Three classes of pollutants generated by wildfires are of particular concern for human health: (1) larger particulate matter represents inhalable particles with an aerodynamic diameter 0 μm or less; (2) fine particulate matter represents inhalable particles with an aerodynamic diameter 2.5 μm or less, and (3) the gaseous compound ozone.[11] Pollutant levels (micrograms/meters^3) are continually sensed by locally placed β-attenuation monitors, and then mathematically converted in the United States to an averaged air quality index for each variable. For each of these pollutants, an air quality index value of greater than 100 defines unhealthy air quality for sensitive groups, with increasing air quality index levels affecting all.[12]

Elevated air quality index is associated with an inflammatory response and respiratory system dysfunction. Numerous studies have shown the impact of poor air quality on asthma exacerbations, emergency department visits, and hospitalizations in both adult and pediatric patients.[13–20] Short-term exposure to wildfire smoke has also been linked to an increase in COVID-19 cases and deaths.[21] Fine particulate matter is the single largest environmental risk factor for human health and death in the United States.[22] Interestingly, fine particulate matter from wildfire smoke may be even more harmful than that from other pollutants, such as automobiles,[23] and even short exposure periods (less than 1 h) have been associated with adverse respiratory outcomes.[24]

Although poor air quality can affect respiratory health, the impact of wildfire smoke in the perioperative setting has not been examined. Pediatric patients are particularly susceptible to adverse respiratory events under general anesthesia, including laryngospasm, bronchospasm, and oxygen desaturation.[25] This is likely due to anatomic and physiologic differences, including smaller airways, higher oxygen consumption, and heightened airway reflexes.[26] Previous studies have demonstrated pediatric-specific risk factors for adverse respiratory events under general anesthesia, including younger age, a history of reactive airway disease, prematurity, the presence of an upper respiratory tract infection, obesity, obstructive sleep apnea, and tobacco smoke exposure in the home.[27] These factors help risk stratify patients presenting for anesthesia,[28] and may impact anesthetic choices. Understanding the effect of the air quality index on the incidence of adverse respiratory events under general anesthesia could be an important factor to help further assess these patients. We hypothesized that an unhealthy air quality index (greater than 100) due to wildfire smoke would increase the risk of an adverse respiratory event under general anesthesia in the pediatric population.

Materials and Methods

After institutional review board approval, we conducted a retrospective double-cohort study of pediatric patients aged 0 to 18 yr who presented for an anesthetic encounter at the University of California, San Francisco, a large tertiary care hospital in geographic proximity to recent major wildfires Written informed consent was waived by our institutional review board, and Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed.[29] Data were acquired from the electronic health record (Epic Systems Corporation, USA). The impact of two significant wildfire events, the Camp Fire in 2018 and the August Complex Fire in 2020 were studied, because these events significantly impacted air quality at our hospital and the surrounding communities. Perioperative records of all noncardiac patients presenting from home for an anesthetic during a 2-week period at the start of each of these fires were reviewed. The Camp Fire study period was defined as November 10, 2018, through November 24, 2018, and the August Complex Fire study period was September 10, 2020, through September 24, 2020. A comparison cohort examined mirroring periods immediately before each fire in October 2018 and August 2020, respectively. The August Complex Fire name is misleading because this wildfire impacted air quality in the Bay Area in September 2020 and did not overlap with our August 2020 control period.

Exclusion criteria included all anesthetics performed for all inpatients, because these patients may not have been exposed to polluted air due to robust hospital filtration systems. We also excluded patients with a history of congenital cardiac disease or patients undergoing cardiac surgery, because preexisting cyanosis may have affected our outcome measures. For patients who had multiple procedures during the time periods of interest, only the first anesthetic per patient was included.

Our exposure variable was the presence of an air quality index greater than 100 for fine particulate matter, larger particulate matter, and/or ozone from the closest air quality sensor to the patient's home within 14 days of their anesthetic encounter. We considered an air quality index greater than 100 for fine particulate matter, larger particulate matter, and/or ozone to represent unhealthy air quality, and an air quality index less than 100 as healthy air quality. All fine particulate matter, larger particulate matter, and/or ozone air quality sensors for states represented in each cohort were queried for daily summary data.[30] With the use of Python, the latitude/longitude of each patient's home address was compared with the latitude/longitude of all sensors, and the closest sensor's data were returned for each sensor type. The median distance of a sensor to a patient's home address was 4.6 miles with an interquartile range of 7.3 miles. A maximum air quality index value for each variable was taken from the closest sensor for the time period 14 days before and including the date of the anesthetic encounter. An air quality index of greater than 100 for any of the three variables (fine particulate matter,

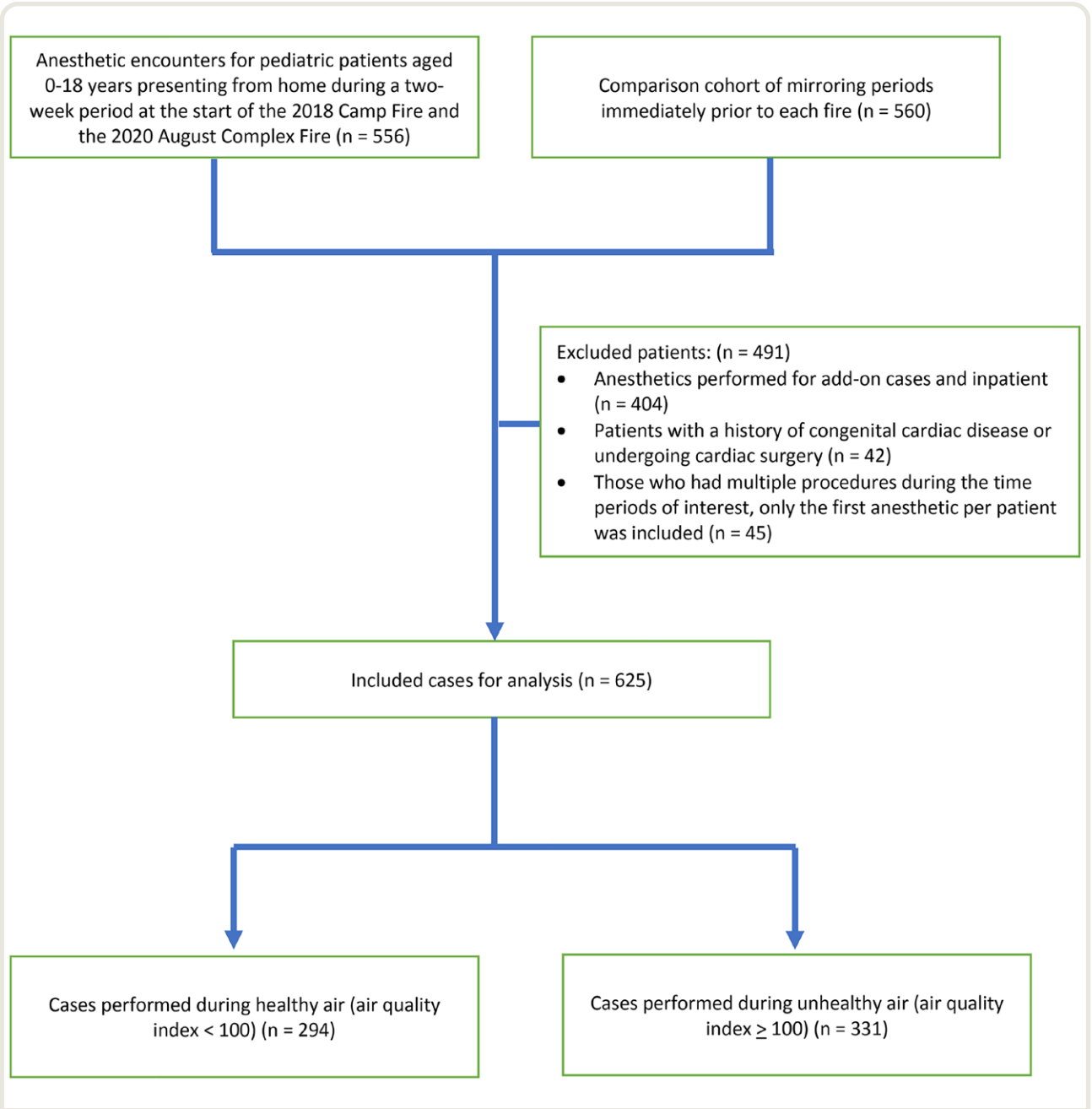

Fig. 1. Flowchart of the retrospective study cohort study.

larger particulate matter, and/or ozone) was considered an exposure, because this value represents a clear demarcation between satisfactory and unhealthy air quality per the Environmental Protection Agency (Washington, DC).

Outcome variables included adverse respiratory events occurring during or immediately after the anesthetic in the recovery room. Adverse respiratory events were defined as bronchospasm, laryngospasm, desaturation (as defined as an Spo_2 value less than 95% for more than 1 min), and reintubation. Anesthetic-related complications were recorded by the anesthesiologist in each medical record and automatically collected. However, because not all of these events are consistently documented in the record, additional markers for adverse respiratory events were considered as surrogates, including the intraoperative administration of inhaled albuterol or intravenous epinephrine (bronchospasm), and the administration of propofol boluses in the recovery room (laryngospasm). Manual chart review was performed to verify each surrogate event. Covariates were collected from the electronic medical record. These included demographic variables (age, sex, body mass index), and the patient's pertinent medical history, including history of prematurity, history of

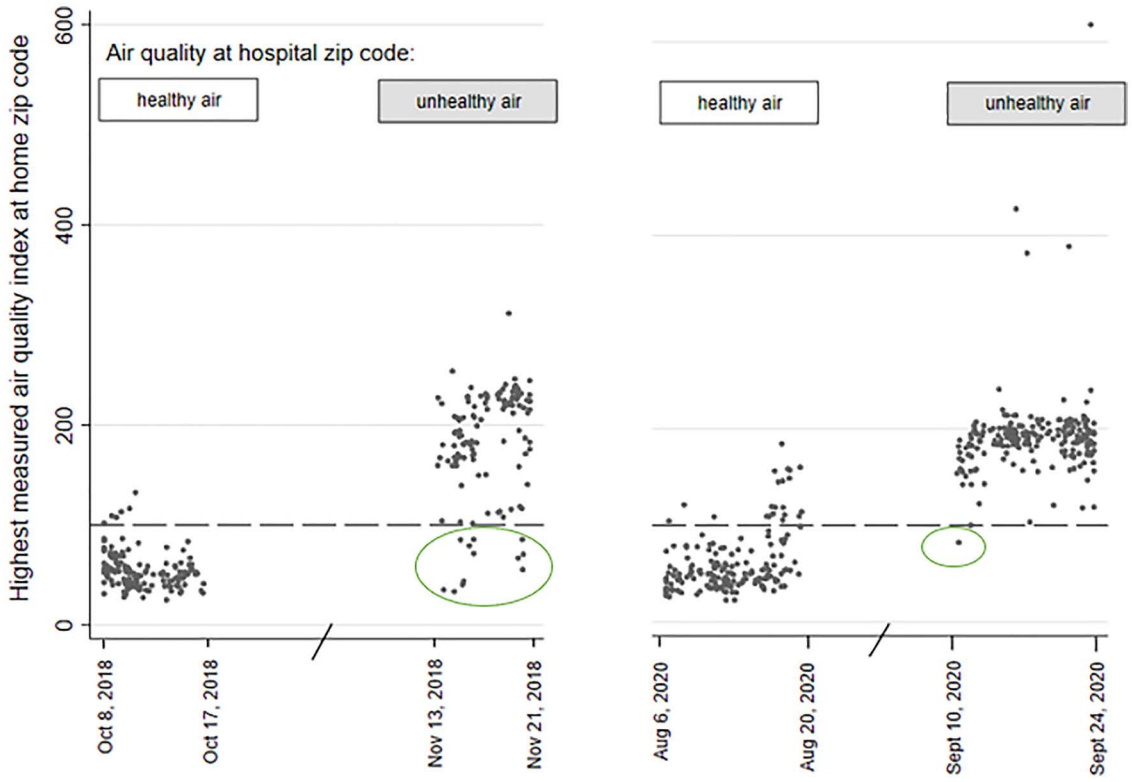

Fig. 2. Time series plotting the highest measured air quality index during study periods. This time-series plots the highest air quality index measurement (small particulate matter, larger particulate matter, or ozone) for each patient at their home zip code during a 2-week period before their surgical procedure on the *y* axis, plotted against the month of their surgical procedure on the *x* axis. During the study periods in October 2018 and August 2020, the highest measured air quality index for any pollutant was less than 100 at the hospital zip code, and the index was 100 or higher during the study months of November 2018 and September 2020. The *dashed line* indicates an air quality index of 100 at home zip code. The *green circles* indicate the 13 patients that were not exposed at their home zip code but were exposed en route to the hospital on their day of the surgical procedure. These 13 patients were reclassified as exposed in the *post hoc* analysis.

reactive airway disease (as a Snomed concept in the patient's chart, or by the use of home pulmonary medications such as albuterol). Additionally, perioperative variables, including the airway device used for the anesthetic (supraglottic airway or endotracheal tube) and the patient's American Society of Anesthesiologists physical status were collected for analysis. Data on home tobacco exposure were not available in the record and could not be analyzed in this study.

Statistical Analysis

All statistical analyses were based on a directed acyclic graph that displayed the relationship between the exposure of interest, the outcome, and covariates.[31,32] The directed acyclic graph was created before data were accessed (Supplemental Figure 1, http://links.lww.com/ALN/C906).

Balance between the study groups was assessed by computing the absolute standardized differences to confirm even distribution of measured demographic and perioperative variables. In general, absolute standardized difference values less than 0.2 are regarded as small, and less than 0.1 as negligible.[33,34] Data are presented as mean ± SD for continuous measures, and n (%) for categorical measures.

Bivariable associations between the study groups were assessed with the chi-square test or the Mann–Whitney U test to confirm even distribution of measured demographic and perioperative variables. Data are presented as median ± interquartile range for continuous measures, and n (%) for categorical measures.

Because wildfires can be described as a natural event and the exposure to them is a random assignment, we have not identified potential confounders to be included in the model.

On the basis of our directed acyclic graph (Supplemental Figure 1, http://links.lww.com/ALN/C906), we identified a potential collider stratification bias: during periods of wildfires, procedures for patients with current respiratory symptoms might have been canceled. Patients with reactive airway disease are at a higher risk for respiratory symptoms during higher air quality index levels, and they are also more susceptible to perioperative airway complications.

Therefore, this high-risk subgroup of patients might be underrepresented in our study cohort. To address this potential collider stratification bias, we have adjusted our analyses for the variable "history of reactive airway disease." Based on these considerations, we fit a generalized linear model for the binomial family. Robust standard errors were calculated using the sandwich estimator of variance. The log link function was used to estimate risk ratios, and the identity link function was used to estimate risk differences. In our model, we specified unhealthy air quality, measured as an air quality index greater than 100, as the exposure variable, adverse respiratory events as the outcome variable, and history of reactive airway disease as adjustment variable.

We further investigated our data for two-way interactions between air quality index group and (1) history of reactive airway disease, (2) prematurity, (3) the type of airway device used, (4) airway surgery, (5) body mass index, and (6) age on perioperative adverse respiratory events by fitting separate binomial regression models, including interaction terms, between those candidate variables and air quality index. All models were adjusted for the history or reactive airway disease as appropriate. Based on these regression models, we generated interaction plots. These plots display the predicted mean percentages of adverse respiratory events per air quality index group for all subgroups.

We report unadjusted incidences of perioperative airway complications overall and per air quality group and stratified by history of reactive airway disease. For the adjusted and subgroup analyses, we chose the risk ratio as our primary measure of effect, but we also reported main effects on an additive scale as risk difference.[35] We then calculated the numbers needed to harm as appropriate. A minimum clinically meaningful effect size was not defined *a priori*.

No statistical power calculation was conducted before the study, because we were restricted based on the wildfire periods, and the sample size was solely based on the available data. A data analysis and statistical plan was written after the data were accessed. All *P* values are drawn for two-sided hypothesis testing, and statistical significance was evaluated at the significance level of 0.05. We used Stata 17 (Stata Corp., USA) for all statistical analyses.

Post Hoc Analysis

During evaluation of our dataset, we found 13 patients that were not exposed to unhealthy air at their home zip code and were therefore classified as nonexposed; however, these patients were exposed to unhealthy air en route to the hospital, based on the air quality index values at the hospital zip code location. Because even short exposures to unhealthy air might affect respiratory health,[24] we performed a sensitivity analysis where we reclassified these 13 pediatric patients as exposed to unhealthy air. We re-ran our primary binomial regression model with this adjusted cohort.

Results

A total of 1116 patients had an anesthetic encounter during the study period, and 556 of these encunters were during a wildfire period; 491 met exclusion criteria, leaving 625 for analysis (fig 1). Baseline characteristics were generally balanced between the healthy air and unhealthy air groups (table 1). No data were missing from the data set. Two hundred ninety-four patients were included in the healthy air group, and 331 patients were included in the unhealthy air group based on patient home zip code (fig. 1). The distribution of air quality index by home zip code largely reflects corresponding time periods of the wildfire periods; however, 13 of 294 patients (4.4%) that were classified in the healthy air group were likely exposed en route to the hospital on their day of surgery (fig. 2). A subsequent *post hoc* analysis was performed for these patients (Supplemental Table 1, http://links.lww.com/ALN/C907).

During the study period, 265 of 625 patients experienced an adverse respiratory event, defined as a composite of laryngospasm, bronchospasm, desaturation, and reintubation. The most common adverse respiratory event was desaturation (n = 255), followed by laryngospasm (n = 12), and then bronchospasm (n = 6). Two of 12 cases of laryngospasm and 5 of 6 cases of bronchospasm were identified by surrogate markers in the medical chart query. Each adverse respiratory event was individually reviewed and manually verified in the medical chart. No cases of reintubation occurred in the study period. The overall risk of an airway complication was 42.4% (265 of 625). Among patients exposed to healthy air, the adverse respiratory event risk was 40.8% (120 of 294), whereas among patients exposed to unhealthy air, the adverse respiratory event risk was 43.8% (145 of 331).

Data were then further analyzed to account for possible selection bias. In our binomial regression model adjusted for a history of reactive airway disease, the risk of airway complications was 1.08 times higher (95% CI, 0.90 to 1.30; $P = 0.401$) during unhealthy air periods compared with healthy air periods.

Stratifying our data by history of reactive airway disease, we found statistically significant interactions (table 2). In children without a history of reactive airway disease, the risk of adverse respiratory events did not change during periods with unhealthy air (40.3%) compared with periods with healthy air (42.0%); the relative risk was 0.96 (0.77 to 1.19, $P = 0.703$). In children with a history of reactive airway disease, the risk of adverse respiratory events increased from 36.8% during healthy air periods to 55.1% during periods with unhealthy air; the relative risk was 1.50 (1.04 to 2.17, $P = 0.032$). The effect of air quality on adverse respiratory events was significantly modified by reactive airway disease status with a relative risk of 1.56 (1.02 to 2.40, $P = 0.041$; (table 2; fig. 2).

Our analysis also showed a significant subgroup effect on the additive scale. The risk difference of the differences

Table 1. Baseline Variables per Study Group

Variables	All Patients (n = 625)	Healthy Air (n = 294)	Unhealthy Air (n = 331)	Absolute Standardized Differences
Age, yr, median (interquartile range)	8.1 (5.5)	7.9 (5.6)	8.3 (5.3)	0.076
Sex, n (%)				0.075
Male	262 (42.9)	129 (43.9)	133 (40.2)	
Female	363 (58.1)	169 (56.1)	204 (59.5)	
American Society of Anesthesiologists physical status, n (%)				0.139
1	189 (30.2)	94 (32.0)	95 (28.7)	
2	315 (50.4)	143 (48.6)	172 (52.0)	
3	96 (15.4)	47 (16.0)	49 (14.8)	
4	1 (0.2)	1 (0.3)	0 (0.0)	
Not recorded	24 (3.8)	9 (3.1)	15 (4.5)	
Body mass index, median (interquartile range)	18 (9.1)	18 (7.6)	19 (10)	0.055
History of reactive airway disease, n (%)				0.010
No	479 (76.6)	226 (76.9)	253 (76.4)	
Yes	146 (23.4)	68 (23.1)	78 (23.6)	
History of prematurity, n (%)				0.059
No	571 (91.4)	266 (90.5)	305 (92.1)	
Yes	54 (8.6)	28 (9.5)	26 (7.9)	
Airway surgery, n (%)				0.118
No	698 (95.7)	285 (96.9)	325 (94.8)	
Yes	27 (4.3)	9 (3.1)	18 (5.4)	
Airway device used, n (%)				0.116
Supraglottic airway	277 (44.3)	127 (43.2)	150 (45.3)	
Endotracheal tube	188 (30.1)	84 (28.6)	104 (31.4)	
Neither recorded	160 (25.6)	83 (28.2)	77 (23.3)	

Data are presented as median (interquartile range) for continuous measures, and n (%) for categorical measures.

Table 2. Subgroup Analysis

	Adverse Respiratory Events		
	Healthy Air	Unhealthy Air	
	n/N (%) Risk ratio (95% CI) *P* Value	n/N (%) Risk ratio (95% CI) *P* Value	Risk ratio (95% CI) by subgroups of reactive airway disease *P* Value
No reactive airway disease	95/226 (42.0) *1.0 (reference)*	102/253 (40.3) 0.96 (0.77–1.19) *P* = 0.703	*0.96 (0.77–1.19)* *P* = 0.703
Reactive airway disease	25/68 (36.8) 0.87 (0.62–1.24) *P* = 0.450	43/78 (55.1) 1.31 (1.02–1.69) *P* = 0.035	1.50 (1.04–2.17) *P* = 0.032

The incidence of perioperative airway complications during healthy and unhealthy air time periods, stratified by history of reactive airway disease. Healthy air as defined by air quality index less than 100. Unhealthy air as defined by air quality index greater than 100. The measure of interaction on the multiplicative scale: Risk ratio 1.56 (1.02 to 2.40, *P* = 0.041). The measure of interaction on the additive scale: Risk difference 20.1% (1.9 to 38.3, *P* = 0.031). The measures of interaction are the ratio/difference between the two subgroup-specific risks displayed in the last column of the table.

N indicates the total number of observations, n is the number of adverse respiratory events.

in adverse respiratory events in the healthy air period *versus* the unhealthy air period between children with and without reactive airway disease was 20.1% (1.9 to 38.3, *P* = 0.031; fig. 3) For the subgroup of children with a history of reactive airway disease, the number needed to harm due to exposure to unhealthy air was 5.5 (95% CI, 2.9 to 41.0).

In our cohort, 54 of 625 pediatric patients (8.6%) were born prematurely. Of those, 32.1% (9 of 28) had an adverse respiratory event documented during healthy air periods, and 57.7% (15 of 26) during unhealthy air periods (adjusted relative risk 1.87 [1.00 to 3.50], *P* = 0.050). In comparison, of patients not born prematurely 41.7% (111 of 266) had an adverse respiratory event during healthy air periods, and 42.6 (130 of 305) had an adverse respiratory event during time periods with unhealthy air (adjusted relative risk 1.02 [0.85 to 1.24], *P* = 0.792). Measures of interaction on the

multiplicative (adjusted risk ratio 1.82 [0.95 to 3.51], P = 0.073), and on the additive scale (adjusted risk difference 25.8% [–1.1 to 52.7], P = 0.060) missed the threshold for statistical significance (table 3; fig. 4).

The tests for interaction did not detect significant subgroup effects between pediatric patients with and without reactive airway disease for exposure status (healthy *versus* unhealthy air exposure) and strata of airway surgery (adjusted risk ratio 1.12 [0.37 to 3.40], P = 0.841), strata of airway device used (adjusted risk ratio for laryngeal mask airway compared with endotracheal tube 1.22 [0.78 to 1.90], P = 0.348), body mass index (adjusted risk ratio 0.99 [0.94 to 1.42], P = 0.165), and age (adjusted risk ratio 1.01 [0.98 to 1.05], P = 0.483).

Post Hoc Analysis

After reclassification of exposure status for 13 patients, the risk of adverse respiratory events was 40.2% (113 of 281) in the healthy air group and 44.2% (152 of 344) in the unhealthy air group. In our binomial regression analysis, the incidence of adverse respiratory events increased in pediatric patients with reactive airway disease (risk ratio 1.57 [1.07 to 2.30], P = 0.021). The test for interaction between pediatric patients with and without reactive airway disease was also significant (risk ratio 1.61 [1.04 to 2.49], P = 0.034). Compared with our primary regression analysis, the effects were slightly more pronounced.

Discussion

Air pollution due to wildfire smoke has unfortunately become a regular occurrence during late summer and fall in the North American West, and increasingly worldwide. These wildfires have significant health risks, especially for vulnerable patient populations. We studied the impact of wildfire smoke on perioperative risk in pediatric patients and found that pediatric patients with an underlying history of reactive airway disease were more likely to experience adverse respiratory events under anesthesia compared with controls during periods of unhealthy air quality as defined by an air quality index greater than 100 for fine particulate matter, larger particulate matter, and/or ozone.

Adverse respiratory events are of significant concern to the anesthesiologists, patients, and their families. Often times, adverse respiratory events do not cause complications, or cause issues of minor clinical significance. Most of the adverse respiratory events in our study were minor and manageable airway complications. However, in rare instances, adverse respiratory events can lead to premature termination of the surgical procedure, prolonged recovery room periods, unanticipated hospital admission, and more

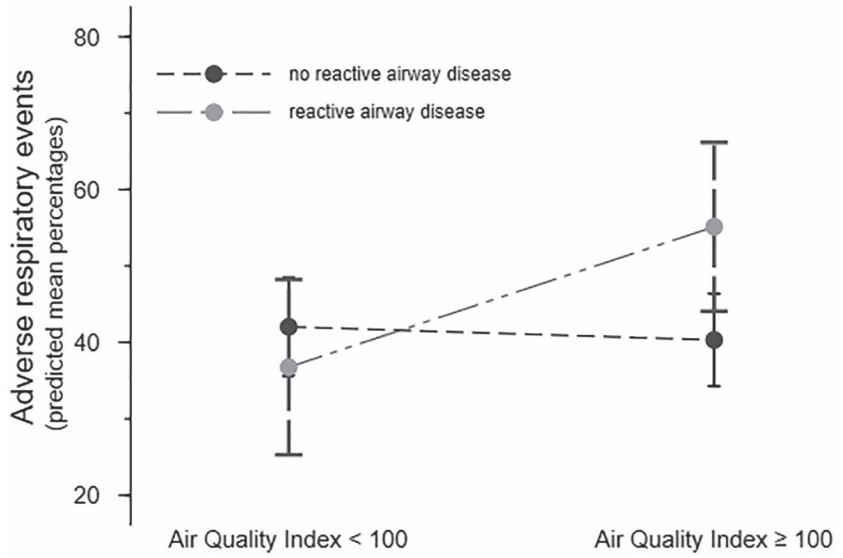

Fig. 3. Interaction plot demonstrating the effects of air quality on predicted adverse respiratory events modified by reactive airway disease status. The figure displays the predicted mean percentages of adverse respiratory events on the *y* axis for each level of air quality index on the *x* axis. The predicted mean of adverse respiratory events is derived from the binomial regression model. The air quality index less than 100 indicates healthy air, and the air quality index 100 or greater indicates unhealthy air. The *gray circles* show the predicted percentages of adverse respiratory events for the subgroup of children with reactive airway disease, and the *black circles* for children with no reactive airway disease. The error bars indicate the CI of the prediction of the mean percentages. The *dashed lines* visualize the change in predicted mean percentages of adverse respiratory events from one level of air quality index to the other. The difference in change between the two subgroups, that is, reactive airway disease *versus* none, is shown as the difference between the two *dashed lines* and is the visual representation of the measure of interaction.

Table 3. Subgroup Analysis

	Adverse Respiratory Events		
	Healthy Air	**Unhealthy Air**	
	n/N (%) Risk ratio (95% CI) *P* Value	n/N (%) Risk ratio (95% CI) *P* Value	Risk ratio (95% CI) by subgroups of reactive airway disease *P* Value
No history of prematurity	111/266 (41.7) *1.0 (reference)*	130/305 (42.6) 1.02 (0.85–1.24) *P = 0.792*	1.02 (0.85–1.24) *P = 0.792*
History of prematurity	9/28 (32.1) 0.74 (0.42 to 1.30) *P* = 0.299	15/26 (57.7) 1.39 (0.98–1.97) *P*= 0.065	1.87 (1.00–3.50) *P* = 0.050

Incidence of perioperative airway complications during healthy and unhealthy air time periods, stratified by prematurity status and adjusted for reactive airways disease status. Healthy air as defined by air quality index less than 100. Unhealthy air as defined by air quality index greater than 100. The model is adjusted for history of reactive airway disease. Measure of interaction on the multiplicative scale: Risk ratio 1.82 (0.95 to 3.51, *P* = 0.073). Measure of interaction on the additive scale: Risk difference 25.8% (–1.1 to 52.7, *P* = 0.060). The measures of interaction are the ratio/difference between the two subgroup-specific risks displayed in the last column of the table.

N indicates the total number of observations, n is the number of adverse respiratory events.

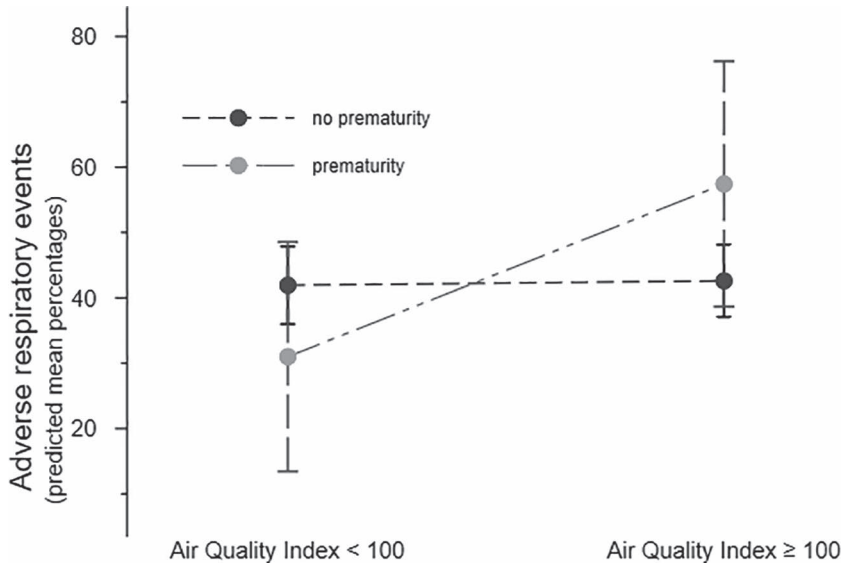

Fig. 4. Interaction plot demonstrating the effects of air quality on predicted adverse respiratory events modified by prematurity status and adjusted for reactive airway disease status. The figure displays the predicted mean percentages of adverse respiratory events on the *y* axis for each level of air quality index on the *x* axis. The predicted mean of adverse respiratory events is derived from the binomial regression model. The air quality index less than 100 indicates healthy air, and the air quality index 100 or greater indicates unhealthy air. The *gray circles* show the predicted percentages of adverse respiratory events for the subgroup of prematurely born pediatric patients, and the *black circles* for pediatric patients not born prematurely. The error bars indicate the CI of the prediction of the mean percentages. The *dashed lines* visualize the change in predicted mean percentages of adverse respiratory events from one level of air quality index to the other. The difference in change between the two subgroups, that is, prematurity *versus* none, is shown as the difference between the two dashed lines and is the visual representation of the measure of interaction.

severe sequelae such as cardiopulmonary arrest. Previous studies have shown that multiple factors can contribute to the risk of an adverse respiratory event under anesthesia, including a current or recent upper respiratory tract infection, a history of prematurity, a history of reactive airway disease, a history of tobacco smoke exposure, planned airway surgery, and endotracheal intubation. Evaluating a patient's respiratory status before anesthesia is essential to assess these risks. When possible, risk factors that are modifiable should be optimized before proceeding with anesthesia.

For example, a child with a respiratory tract infection who presents for an elective procedure can have the procedure delayed until all respiratory symptoms are resolved.[36]

Our data suggest that the presence of unhealthy air due to wildfire smoke may also be a modifiable risk factor for an adverse respiratory event under anesthesia for children with an underlying history of reactive airway disease or prematurity. In our study group, patients with an underlying history of reactive airway disease were 1.5 times more likely to experience an adverse respiratory event during periods of unhealthy air compared with periods with healthy air. This effect was demonstrated after accounting for the fact that it is possible that some patients with underlying reactive airway disease may have had their procedure canceled due to respiratory symptoms during periods of unhealthy air. With a number needed to harm of only 5.5, surgical postponement may be an important consideration for vulnerable patients during periods of unhealthy air.

In this study, we had an overall adverse respiratory event rate of 42.4%. This rate is consistent with other reported rates of adverse respiratory events in the pediatric anesthesia literature.[37–39] The most common adverse respiratory event was desaturation, defined by an oxygen saturation less than 95% for 1 min. Although we did not collect data on the method of anesthesia induction (intravenous *vs*. inhalational), a recent meta-analysis demonstrated no significant difference in the occurrence of adverse respiratory events between inhalation and intravenous induction.[40] Other potential variables that may have impacted the adverse respiratory event risk in our study, including patient age, type of procedure, type of airway device used, and body mass index, did not impact the incidence of adverse respiratory event in either of the two groups. Both study periods also occurred in the fall, when upper respiratory tract infections may be more common in pediatric populations, which may explain the relatively high incidence.

We chose to analyze a 2-week period after each fire in this study. Previous literature has demonstrated that chemical irritants such as particulate matter and ozone cause airway epithelial damage and sensitize airway receptors to become prone to bronchospasm,[41] and that these changes may persist for weeks to months after exposure.[42] Although the exact duration of this sensitization period has not been precisely defined, we chose to analyze subjects for a 14-day period after each fire outbreak to ensure that subjects had been exposed to unhealthy air in a short time period before presenting for anesthesia. A healthy air control group was examined for each fire period because the two fires straddled the outbreak of the COVID-19 pandemic. COVID-19 influenced both our surgical volume and our surgical case mix in 2020 and may have altered the incidence of adverse respiratory events in each group.

Preterm delivery has been associated with the development of reactive airway disease later in life.[43] In our study, pediatric patients with a history of prematurity were also affected by unhealthy air quality. Unfortunately, our sample size for this patient population was very small, limiting the power of the study for this group of patients.

Our study has several limitations. It is a retrospective study, and therefore all adverse respiratory events may not have been reliably captured. All bronchospasm and laryngospasm events identified by the anesthesiologist in the medical record were included in in this study. However, not all incidences may have been reported if quickly resolved. We therefore used surrogate measures, including the use of intraoperative and postoperative albuterol (as a marker of bronchospasm), as well as the use of propofol in the recovery room (as a marker of laryngospasm) to capture adverse respiratory events. Each of these surrogate events were confirmed *via* chart review to exclude overestimation of true complications when possible. Despite this, either underestimation or overestimation of true complications may have occurred. Additionally, reporting bias may have occurred, with anesthesiologists disproportionately underreporting events in healthy patients compared with their nonhealthy counterparts. The majority of the adverse respiratory events were minor and manageable airway complications. Furthermore, due to the retrospective nature of this study, some datapoints were not obtainable.

In this study, we used air quality index numbers at the patients' home addresses for the purposes of determining healthy air and unhealthy air. We have no way of knowing for sure if the patients were residing at their home addresses before their surgery. At our hospital, a composite air quality index of greater than 100 was present in 12 days in the 2018 wildfire period and 5 days in the 2020 wildfire period. Because all patients were ambulatory, contact with unhealthy air for at least a minimal period on these days was likely on their day of surgery. With our data we cannot exclude that the association between unhealthy air exposure and adverse respiratory events in children with reactive airway disease was driven by the double exposure to unhealthy air at home as well as en route to the hospital. In our cohort there were 12 children in 2018 and 1 child in 2020 that were not exposed to unhealthy air at their home area (therefore classified as unexposed), but they were exposed to unhealthy air en route to the hospital on the day of surgery (Supplemental Table 1, http://links.lww.com/ALN/C907). We therefore performed a *post hoc* sensitivity analysis with reclassification of these 13 children as "exposed to unhealthy air," and we found a slightly stronger association between exposure to unhealthy air and perioperative respiratory adverse events in children with a history of reactive airway disease. The fact that we see a slightly stronger association when we reclassify the children with a single exposure en route to the hospital as exposed supports an assumption that double exposure is not the main driver of the effect.

Data regarding the use of high-quality masks/respirators or home air filtration were not available. We did not have reliable data about the presence or absence of a recent upper

respiratory tract infection for each subject, so we were unable to assess the impact of upper respiratory tract infections as a risk factor in this study. Additionally, known home tobacco use, a recognized risk factor for adverse respiratory events, was unable to be assessed *via* the electronic record. Provider experience level data were not collected for this study. An air quality index threshold of greater than 100 was chosen for our study because this is in line with the national ambient air quality standard, set by the Environmental Protection Agency. Unfortunately, our sample size was insufficient to assess the air quality index as a linear variable. Finally, this study was limited to a single center, although we hope to broaden our study to include other tertiary pediatric medical centers affected by wildfire smoke in the near future.

In sum, unhealthy air, a measured by an air quality index greater than 100 for particulate matter or ozone, may increase the incidence of adverse respiratory events during anesthesia in pediatric patients who have underlying risk factors. In this patient population, the presence of unhealthy air may represent an additional risk factor that should be considered by the anesthesiology team. Anesthesiologists should be aware of the increased risk and be prepared for complications; the presence of multiple other risk factors during periods of unhealthy air may warrant postponing elective procedures. Because wildfires are growing in both frequency and severity, they may have an increasing impact on the perioperative care of pediatric patients. It is important for anesthesiologists to recognize the impact of unhealthy air on vulnerable populations.

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Competing Interests

Dr. Ferschl has been a paid speaker for The American Physician Institute (Chicago, Illinois) and The California Society of Anesthesiologists (Poipu, Hawaii). Dr. Robinowitz is an unpaid specialty board member for Epic Anesthesia (Madison, Wisconsin) and receives complimentary registration for Epic conferences. The other authors declare no competing interests.

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Supplemental Digital Content

Figure 1: Directed Acyclic Graph, http://links.lww.com/ALN/C906

Table 1: Sensitivity Analysis of Subgroup Analysis, http://links.lww.com/ALN/C907

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ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

A Beautiful Anesthetic, Methyl Chloride in the Belle Époque

Not merely a destination for elites seeking the art and culture of the Belle Époque ("beautiful era"), Paris was a European center for medical education in the mid- to late 19th century. In contrast to lab- and lecture-based medical schooling in the United States, Parisian academe provided access to hospital patients, live surgical demonstrations, and cadaver dissections. In Paris, methyl chloride was pioneered as a local anesthetic and novel treatment for neuralgias. Skilled Parisian instrument makers such as Mariaud built siphons to store and dispense that volatile solution. A typical device, the methyl chloride siphon, is pictured above (*boxed, right*). Popular in the 1890s, the black cylinder was filled with volatile liquid and stored under pressure. Dispensed in a stream through a nozzle, the methyl chloride evaporated on the skin (*left*) to topically relieve neuralgias or to provide local anesthesia for minor surgeries. These siphons were such well-constructed devices that they were frequently repurposed for laboratory use. Fortunately, the Wood Library-Museum found this one intact. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology. www.woodlibrarymuseum.org)

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