

Prospective Multicenter Study of Children With Bronchiolitis Requiring Mechanical Ventilation



WHAT'S KNOWN ON THIS SUBJECT: Bronchiolitis is one of the most common infectious respiratory conditions of early childhood, and most children have a mild clinical course. Unfortunately, the small subgroup of children requiring continuous positive airway pressure and/or intubation remains ill-defined.



WHAT THIS STUDY ADDS: In children with bronchiolitis, we found several demographic, historical, and clinical factors that predicted the need for mechanical respiratory support including in utero smoke exposure. We also found a novel subgroup of children with bronchiolitis who have a rapid respiratory decline.

abstract



OBJECTIVE: To identify factors associated with continuous positive airway pressure (CPAP) and/or intubation for children with bronchiolitis.

METHODS: We performed a 16-center, prospective cohort study of hospitalized children aged <2 years with bronchiolitis. For 3 consecutive years from November 1 until March 31, beginning in 2007, researchers collected clinical data and a nasopharyngeal aspirate from study participants. We oversampled children from the ICU. Samples of nasopharyngeal aspirate were tested by polymerase chain reaction for 18 pathogens.

RESULTS: There were 161 children who required CPAP and/or intubation. The median age of the overall cohort was 4 months; 59% were male; 61% white, 24% black, and 36% Hispanic. In the multivariable model predicting CPAP/intubation, the significant factors were: age <2 months (odds ratio [OR] 4.3; 95% confidence interval [CI] 1.7–11.5), maternal smoking during pregnancy (OR 1.4; 95% CI 1.1–1.9), birth weight <5 pounds (OR 1.7; 95% CI 1.0–2.6), breathing difficulty began <1 day before admission (OR 1.6; 95% CI 1.2–2.1), presence of apnea (OR 4.8; 95% CI 2.5–8.5), inadequate oral intake (OR 2.5; 95% CI 1.3–4.3), severe retractions (OR 11.1; 95% CI 2.4–33.0), and room air oxygen saturation <85% (OR 3.3; 95% CI 2.0–4.8). The optimism-corrected c-statistic for the final model was 0.80.

CONCLUSIONS: In this multicenter study of children hospitalized with bronchiolitis, we identified several demographic, historical, and clinical factors that predicted the use of CPAP and/or intubation, including children born to mothers who smoked during pregnancy. We also identified a novel subgroup of children who required mechanical respiratory support <1 day after respiratory symptoms began. *Pediatrics* 2012;130:e492–e500

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KEY WORDS

bronchiolitis, continuous positive airway pressure, intubation, ICU, respiratory syncytial virus, human rhinovirus

ABBREVIATIONS

CI—confidence intervals
CPAP—continuous positive airway pressure
ED—emergency department
HRV—human rhinovirus
IQR—interquartile ranges
MARC—Multicenter Airway Research Collaboration
NPA—nasopharyngeal aspirate
OR—odds ratio
PCR—polymerase chain reaction
RSV—respiratory syncytial virus

Drs Mansbach, and Piedra, Ms Sullivan, and Dr Camargo were responsible for study concept and design; Drs Mansbach, Piedra, and Stevenson, Ms Sullivan, Mr Forgey, Ms Espinola, and Dr Camargo were responsible for acquisition of data; Drs Mansbach, Piedra, Stevenson, and Clark, Ms Espinola, and Dr Camargo were responsible for analysis and interpretation of data; Drs Mansbach, and Clark, Ms Espinola, and Dr Camargo drafted the manuscript; Drs Mansbach, Piedra, and Stevenson, Ms Sullivan, Mr Forgey, Dr Clark, Ms Espinola, and Dr Camargo were responsible for critical revision of the manuscript for important intellectual content; and all authors were responsible for final approval of version to be published.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-0444

doi:10.1542/peds.2012-0444

Accepted for publication Apr 23, 2012

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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Bronchiolitis is one of the most common infectious respiratory conditions of early childhood^{1,2} and is associated with multiple different viruses.³ Most children who develop bronchiolitis have a mild course, but 2% to 3% of children with bronchiolitis are hospitalized^{4,5} and <1% are admitted to an ICU, are intubated, or die.^{6–9} Despite objective physical examination findings for respiratory distress (eg, respiratory rate and degree of retractions), the difficulty and uncertainty of determining the appropriate level of supportive care for children with bronchiolitis is well documented by marked variability in acute care and disposition.^{7,10–12} One reason for this variability may be that the clinical course for children with bronchiolitis tends to be variable and dynamic.¹³

Indeed, the subgroup of children with severe bronchiolitis requiring continuous positive airway pressure (CPAP) and/or intubation remains ill defined. This lack of understanding may hinder treatment advances, as well as mechanistic research, because this group of children may respond differently to medications and/or have different long-term clinical outcomes.^{14,15} Researchers have identified demographic, environmental, medical history, and laboratory risk factors for severe bronchiolitis^{1,5,8,16–24} in single-center studies,^{25–28} retrospectively,^{28,29} in children with respiratory syncytial virus (RSV) only,⁶ and in children with RSV before the use of palivizumab.^{6,25} In contrast, we performed a prospective, multicenter, multiyear study of >2000 children hospitalized with bronchiolitis to investigate the historical, environmental, clinical, and pathogenic factors associated with CPAP and/or intubation. We hypothesized that children aged <2 months, with low birth weight, and with preadmission room air oxygen saturation <90% would predict the need for CPAP and/or intubation.

METHODS

Study Design

We conducted a prospective, multicenter cohort study for 3 consecutive years during the 2007 to 2010 winter seasons as part of the Multicenter Airway Research Collaboration (MARC), a program of the Emergency Medicine Network (www.emnet-usa.org). The number of participating sites varied over the 3 years: 13 sites in year 1; 16 sites in year 2; and 14 sites in year 3. Each month from November 1 until March 31, site investigators across 12 US states used a standardized protocol to enroll a target number of consecutive patients from the inpatient wards and the ICU. We aimed to enroll 20% of our total sample from the ICU. To oversample children in the ICU, the ward and ICU enrollments were separate. Once the site reached its target enrollment for that month, the investigators would stop enrollment until the beginning of the following month.

All patients were treated at the discretion of the treating physician. Inclusion criteria were an attending physician's diagnosis of bronchiolitis, age <2 years, and the ability of the parent/guardian to give informed consent. The exclusion criteria were previous enrollment and transfer to a participating hospital >48 hours after the original admission time. All consent and data forms were translated into Spanish. The institutional review board at each of the 16 participating hospitals approved the study.

Data Collection

Investigators conducted a structured interview that assessed patients' demographic characteristics, medical and environmental history, duration of symptoms, and details of the acute illness. The interview included the question, "Did the mother of [child] smoke cigarettes during the pregnancy?" Relevant comorbid medical disorders included review of respiratory, cardiac, neurologic,

gastrointestinal, and immunologic diseases. Emergency department (ED) and daily hospital clinical data, including respiratory rates, daily respiratory rate trends, clinical assessment of degree of retractions (collapsed for analysis into none, mild, and moderate/severe), oxygen saturation, daily oxygen saturation trends, medical management, and disposition were obtained by chart review. These data were manually reviewed at the Emergency Medicine Network Coordinating Center, and site investigators were queried about missing data and discrepancies identified by these manual data checks.

Nasopharyngeal Aspirate Collection and Virology Testing

Nasopharyngeal aspirates (NPAs) were performed by using a standardized protocol. Designated site personnel were trained by use of a lecture, written instructions, and video. All of the sites used the same collection equipment (Medline Industries, Mundelein, IL) and collected 98% of the samples within 24 hours of a child's arrival on the medical ward or ICU. Once collected, the NPA sample was added to transport medium. After collection, the NPA samples were immediately placed on ice and then stored at -80°C . Frozen samples were batch shipped on dry ice overnight to the central laboratory at Baylor College of Medicine, where they were stored at -80°C .

Polymerase Chain Reaction Assay

All polymerase chain reaction (PCR) assays were conducted as singleplex or duplex 2-step real-time PCR. Real-time reverse transcriptase PCR was used for the detection of RSV types A and B, human rhinovirus (HRV), parainfluenza virus types 1, 2, and 3, influenza virus types A and B, 2009 novel H1N1, human metapneumovirus, coronaviruses NL-63, HKU1, OC43, and 229E, enterovirus, adenovirus, *Mycoplasma pneumoniae*, and *Bordetella pertussis*. These tests

are routinely conducted in the central laboratory of one of the investigators (P. A.P.) and details of the primers and probes have been described.^{30–32} All real-time reverse transcriptase-PCR assays were tested in duplicate, and samples with incongruent values were retested.

Statistical Analyses

All analyses were performed by using Stata 11.2 (Stata Corp, College Station, TX). Data are presented as proportions with 95% confidence intervals (95% CIs) and medians with interquartile ranges (IQR).

We performed univariate analyses by using χ^2 , Fisher exact test, and Kruskal-Wallis test, as appropriate. All *P* values were 2-tailed, with *P* < .05 considered statistically significant. Multivariable logistic regression was conducted to evaluate independent predictors of CPAP/ intubation, defined as any instance of patient requiring CPAP and/ or intubation during the admission. We used CPAP/intubation as the outcome of interest because this outcome has less variability than admission to the ICU.^{33–36} Factors were tested for inclusion in the model if they were found to be associated with the outcome in unadjusted analyses (*P* < .20) or were considered potentially clinically significant. An optimism-corrected c-statistic was used to determine model discrimination,³⁷ and the Hosmer-Lemeshow test was used to determine model calibration.³⁸ The final regression model accounts for potential clustering by site and was validated by using bootstrapping.³⁷ The full model was bootstrapped 1000 times and bias-corrected and accelerated 95% CIs were obtained. Results are reported as odds ratios (ORs) with bias-corrected and accelerated 95% CI.

In addition, we used descriptive statistics to better characterize the group of children whose condition declined rapidly. These children began experiencing

difficulty breathing <1 day before the ED visit (as reported by parents/caregiver) and required CPAP/intubation on the first day of their inpatient stay.

RESULTS

Of the 2207 enrolled children, 379 (17%) were enrolled in the ICU. Of these 379 children, 161 (42%) required CPAP and/ or intubation. Of these 161 children, 59 (37%) required CPAP, 64 (40%) were intubated, and 38 (23%) had both CPAP and intubation. Overall, the median age of the 2207 enrolled children was 4 months (IQR, 2–9 months); 61% were born in fall or winter months (October to March); 59% were male; and 61% were white (Table 1). Most children had nonprivate health insurance, were born term, had a birth weight of ≥ 7 pounds, were breastfed, and had no parental history of asthma. The most frequently detected pathogens among enrolled children were RSV-A (43%), RSV-B (30%), and HRV (26%). The median overall hospital length of stay was 2 days (IQR, 1–4 days).

Unadjusted associations between demographic and clinical characteristics and needing CPAP/intubation during the inpatient stay are presented in Table 2. In general, the children most likely to require CPAP/intubation were younger, born between the months of October and March, nonblack race, had a gestational age of 32 to 36 weeks, a birth weight <7 pounds, and began experiencing difficulty breathing <1 day before coming to the ED. Furthermore, clinical factors recorded during the ED visit such as apnea, lower weight, faster pulse, severe retractions, lower oxygen saturations, inadequate oral intake, and nonnormal chest x-ray results all were associated with CPAP/ intubation. Furthermore, oxygen saturation, retractions, and oral intake were significantly associated with each other (*P* < .001 for all associations). No association was detected between the

most common viruses, including coinfections, and CPAP/intubation.

The bootstrapped multivariable logistic regression model for CPAP/intubation is shown in Table 3. Controlling for 10 demographic and clinical characteristics as well as clustering by site, significant independent predictors of CPAP/intubation were as follows: age <6 months, birth weight <7 pounds, maternal smoking during pregnancy, onset of breathing difficulties <1 day before ED visit, presence of apnea, presence of severe retractions, oxygen saturation <85%, and inadequate oral intake. Gender and race were not associated with CPAP/intubation. The optimism-corrected c-statistic for the final model was 0.80, and the Hosmer-Lemeshow test demonstrated a good model fit (*P* = .65).

Of the 161 children requiring CPAP/ intubation, 42 (26%) were identified as having rapidly declined (ie, breathing difficulties began <1 day from the ED visit and needed CPAP/intubation on the first day of their hospitalization). Among these 42 children with rapidly deteriorating conditions, 50% were <2 months of age, 60% were male, 60% were white, and 55% were Hispanic. In addition, 55% had a birth weight of <7 pounds, 38% had apnea, 29% had severe retractions, 11% had an oxygen saturation of <85%, 69% were noted to have inadequate oral intake, 50% were positive for RSV-A, and only 1 child was reported to have normal chest x-ray results. A separate, but overlapping group of children were those requiring mechanical respiratory support on the first day of their hospitalization no matter when the breathing difficulty began (ie, <1 day or ≥ 1 day). Compared with the group of children who needed CPAP/intubation after day 1 of hospitalization, the children requiring CPAP/intubation on day 1 were more likely to have RSV-A (51% vs 31%, *P* = .03) and apnea (36% vs 3%; *P* < .001).

DISCUSSION

In this large, multicenter, multiyear prospective study of children hospitalized with bronchiolitis, we found several factors independently associated with a child's need for CPAP and/or intubation: young age, low birth weight, child of mother who smoked during pregnancy, onset of respiratory symptoms <1 day before presentation, presence of apnea, severe retractions, room air oxygen saturation <85%, and inadequate oral intake. Although viral etiology was not predictive of the need for mechanical respiratory support overall, RSV-A was more common in those children requiring CPAP/intubation on day 1 of hospitalization. Furthermore, these data build on and corroborate previous findings about the severe respiratory ramifications of smoke exposure in utero, a finding of public health importance. A novel finding of clinical and research importance was the identification of a subgroup of children that rapidly declined from the onset of respiratory symptoms at home to requiring CPAP and/or intubation.

Previous studies have examined risk factors for hospitalization,^{6,28,39-42} ICU admissions,¹⁶ CPAP,⁴³ and intubation.^{6,29,44,45} However, of the studies that used CPAP or intubation as the outcome, 3 were retrospective, single-center studies.^{29,43,44} Furthermore, the 2 prospective intubation studies had sample sizes of 63⁶ and 19⁴⁵ children and only included children with RSV. These comprehensive, prospective, multicenter data examining 161 children requiring CPAP and/or intubation have confirmed some previous findings, challenged others, and revealed new findings that deserve attention.

Two of the most consistently identified risk factors for severe bronchiolitis are young age and low birth weight. Regarding young age, several studies have identified age <6 weeks as predictive of severe bronchiolitis,^{6,46,47} but

TABLE 1 Demographic Characteristics, Medical History, and Clinical Presentation of Children With Bronchiolitis, *n* = 2207

Characteristics	<i>n</i>	%
Age in months		
<2	628	28
2-5.9	777	35
6-11.9	491	22
≥12	311	14
Month of birth		
October-March	1345	61
April-September	862	39
Gender		
Male	1311	59
Female	896	41
Race		
White	1357	61
Black	539	24
Other or missing	311	14
Hispanic	802	36
Insurance		
Nonprivate	1494	69
Private	684	31
Gestational age, wk		
<32	142	6
32-36	391	18
≥37 or term	1660	76
Birth weight, lbs		
<5	281	13
≥5	768	35
≥7	1132	52
Mother's age, median (IQR)	2198	27 (23-33)
Is or was breastfed	1334	61
Smoked during pregnancy	334	15
Exposure to smoke	284	13
Family history of asthma		
Neither parent	1486	67
Either mother or father	594	27
Both parents	87	4
Don't know/missing	40	2
History of infant wheezing	498	23
History of infant eczema	334	15
History of infant intubation	225	10
Major, relevant, comorbid medical disorder	460	21
When difficulty breathing began (preadmission)		
≥1 d	1539	71
<1 d	590	27
No difficulty preadmission	47	2
Presence of apnea (chart)	153	7
Weight (lbs), median (IQR)	2152	13 (9-18)
Temperature (F), median (IQR)	2170	99.5 (98.6-100.6)
Pulse (beats per min), median (IQR)	2177	161 (148-176)
Respiratory rate (breaths per min), median (IQR)	2185	48 (40-60)
Retractions		
None	483	22
Mild	925	42
Moderate	554	25
Severe	87	4
Missing	158	7
Oxygen saturation by pulse oximeter or ABG		
<85	89	4
85-87.9	66	3
88-89.9	96	4
90-93.9	362	17
≥94	1546	72

TABLE 1 Continued

Characteristics	n	%
Oral intake		
Adequate	955	43
Inadequate	938	43
Missing	314	14
WBC, median (IQR)	856	11 (9–15)
Platelets, median (IQR)	842	396 (314–490)
Sodium, median (IQR)	631	138 (136–139)
Adenovirus	173	8
<i>B pertussis</i>	4	0.2
Coronavirus-229e	29	1.3
Coronavirus-HKU1	39	1.8
Coronavirus-NL63	31	1.4
Coronavirus-OC43	57	3
Enterovirus	107	5
Influenza-A	14	0.6
Influenza-B	5	0.2
HMPV	155	7
HRV	564	26
<i>M pneumoniae</i>	19	0.9
Novel H1N1 ^a	7	0.3
PIV1	17	0.8
PIV2	11	0.5
PIV3	30	1.4
RSV-A	940	43
RSV-B	664	30
Atelectasis on chest x-ray	272	12
Infiltrate on chest x-ray	285	13
Hyperinflated on chest x-ray	384	17
Peribronchial cuffing on chest x-ray	399	23
Normal chest x-ray	314	14

ABG, arterial blood gas; HMPV, human metapneumovirus; PIV, parainfluenza virus; WBC, white blood count.

^a Only checked in year 3 when novel H1N1 was circulating (n = 854).

we found that, although children <2 months had the highest odds of requiring CPAP/intubation, children up to age 6 months also had an increased odds compared with children >1 year of age. In terms of birth weight, Rietveld and colleagues' retrospective study comparing 2469 children hospitalized with RSV with 140 661 children with RSV infection who were not hospitalized found multivariable ORs similar to our data for children ≤2.5 kg (adjusted OR, 1.7; 95%CI, 1.5–2.0) and >2.5 to 3.0 kg (adjusted OR, 1.3; 95%CI, 1.1–1.4).⁴²

On initial presentation, the clinical factors of apnea, severe retractions, room air oxygen saturation <85%, and inadequate oral intake all independently predicted the need for CPAP and/or intubation. These 4 factors clearly paint the picture of an infant in respiratory distress and, although beyond the scope of this analysis, may be

markers for children who are born with reduced lung function.^{48–50} One of these 4 factors is apnea, and we found in a previous prospective study that apnea in the ED was associated with ICU admission.¹⁶ Similarly, a retrospective chart review study of 185 children aged <12 months with RSV bronchiolitis by Kneyber and colleagues²¹ found that children with apnea were more likely to be intubated. These prospective data confirm that apnea is a serious event in children with bronchiolitis and predicts the need for CPAP and/or intubation. Another factor of interest was room air oxygen saturation. Compared with the referent room air oxygen saturation value of >94%, oxygen saturation values between 85% and 93.9% were not predictive of CPAP/intubation. However, children with <85% oxygen saturation were more likely to require CPAP and/or intubation, and this value is lower

than the previously identified value of 90%, which represents the inflection point on the oxyhemoglobin dissociation curve.⁶ These oxygen saturation data provide a different, less conservative perspective about the severity of a child's bronchiolitis illness that may help to more appropriately triage children to intensive care.

Also of interest were the factors not associated with the need for mechanical respiratory support. For example, previous studies suggest that boys are more likely than girls to have severe bronchiolitis,^{5,9} but in the present data we did not find an association between gender and the severe bronchiolitis outcome, defined as requiring CPAP and/or intubation. Regarding the viral etiology of bronchiolitis, some data suggest that RSV-A^{24,25} and viral coinfections^{51,52} are associated with more severe bronchiolitis symptoms. We found that RSV-A is more common in children requiring CPAP/intubation on the day of admission, but not more common overall among children requiring mechanical respiratory support. Moreover, our previous data identify that children with RSV/HRV coinfections have a protracted severe illness, but not necessarily a higher intensity of illness as represented by intensive care outcomes, such as CPAP/intubation.³

Children born to mothers who smoked during pregnancy have impaired lung function at birth⁵³ that has been shown to persist through childhood.^{54,55} Furthermore, smoke exposure increases the incidence and severity of bronchiolitis.^{19,56–58} Our smoke exposure data extend these findings and are the first to demonstrate that maternal smoking during pregnancy is independently associated with bronchiolitis requiring CPAP and/or intubation even after controlling for 9 other factors. Different mechanisms for the harmful effects of smoke exposure have been examined, but they are beyond the

scope of this analysis.^{59,60} These data clearly demonstrate the respiratory risks associated with in utero smoke exposure and reemphasize the priority that should be placed on smoking cessation, especially in pregnant women.⁶¹ Another interesting finding is that almost 40% of the children who required mechanical respiratory support on the day of presentation had difficulty breathing for <1 day before presentation. Fortunately, no child in our study died. Nevertheless, it is informative to compare the tempo of respiratory decline in this subgroup of children with bronchiolitis with descriptions of children with influenza who died during 2 recent influenza seasons. Bhat and colleagues⁶² described that, during the 2003–2004 influenza season, 29% of children died within 3 days of the onset of illness and 5% died within 1 day. In addition, in a description of the 2009 novel H1N1 pandemic in Argentina, Libster and colleagues⁶³ described that 3 children (23%) died within 3 days of the onset of symptoms. Although there are few data on this topic, high levels of cytokines have been associated with reduced severity of illness in bronchiolitis,^{64,65} which is the opposite for influenza.⁶⁶ Further study on the acute immune responses of this subgroup of children who have rapid respiratory decline may provide further insight into how RSV and HRV pathogenesis may differ from influenza in infants.

The current study has potential limitations. The study participants were enrolled in academic medical centers, and, therefore, these results may not be generalizable to community medical centers. Furthermore, there is institutional variability in care and resource utilization, including CPAP and intubation, for children with bronchiolitis not explained by severity of illness.⁷ Commenting on the appropriateness of these procedures is beyond the scope of these data. However, CPAP and

TABLE 2 Demographic Characteristics, Medical History, and Clinical Presentation of Children With Bronchiolitis by CPAP and/or Intubation Status

Characteristics	No CPAP/Intubation (n = 1998), %	CPAP/Intubation (n = 161), %	P
Age in months			
<2	27	46	<.001
2–5.9	35	34	
6–11.9	23	14	
≥12	15	6	
Month of birth			.002
October–March	60	73	
April–September	40	27	
Gender			.67
Male	59	61	
Female	41	39	
Race			.01
White	61	64	
Black	25	16	
Other or missing	14	20	
Hispanic	36	43	.07
Insurance			.65
Nonprivate	69	67	
Private	31	33	
Gestational age, wk			.02
<32	7	5	
32–36	17	26	
≥37 or term	76	69	
Birth weight, lbs			.01
<5	13	16	
≥5	35	42	
≥7	53	42	
Mother's age, median (IQR)	27 (23–33)	28 (23–33)	.61
Is or was breastfed	61	57	.28
Smoked during pregnancy	15	19	.12
Exposure to smoke	13	11	.38
Family history of asthma			.73
Neither parent	67	66	
Either mother or father	27	30	
Both parents	4	2	
Don't know/missing	2	2	
History of infant wheezing	23	19	.22
History of infant eczema	16	11	.10
History of infant intubation	10	11	.67
Major, relevant, comorbid medical disorder	22	17	.16
When difficulty breathing began (preadmission)			.003
≥1 d	71	59	
<1 d	26	39	
No difficulty preadmission	2	2	
Presence of apnea (chart)	5	28	<.001
Weight (lbs), median (IQR)	13 (9–18)	10 (7–14)	<.001
Temperature (F), median (IQR)	99.5 (98.6–100.6)	99.4 (98.2–100.7)	.17
Pulse (beats per min), median (IQR)	160 (147–175)	173 (155–184)	<.001
Respiratory rate (breaths per min), median (IQR)	48 (40–60)	50 (40–60)	.17
Retractions			<.001
None	22	15	
Mild	43	21	
Moderate	25	34	
Severe	3	20	
Missing	7	10	
Oxygen saturation by pulse oximeter or ABG			<.001
<85	3	17	
85–87.9	3	6	
88–89.9	4	6	
90–93.9	17	16	

TABLE 2 Continued

Characteristics	No CPAP/Intubation (n = 1998), %	CPAP/Intubation (n = 161), %	P
≥94	73	55	
Oral intake			<.001
Adequate	45	20	
Inadequate	41	63	
Missing	14	16	
WBC, median (IQR)	11 (9–15)	11 (9–15)	.59
Platelets, median (IQR)	395 (311–488)	413 (325–517)	.12
RSV-A	42	45	.57
RSV-B	30	29	.81
HRV	25	27	.73
Atelectasis on chest x-ray	11	27	<.001
Infiltrate on chest x-ray	12	29	<.001
Hyperinflated on chest x-ray	17	20	.28
Peribronchial cuffing on chest x-ray	22	25	.53
Normal chest x-ray	15	6	.001

ABG, arterial blood gas; WBC, white blood count.

intubation are major interventions with associated complications,^{33–36} and this outcome should have less practice variability than admission to the ICU. In addition, this was an observational study, and, therefore, the chest radiographs were not performed systematically. Despite our intriguing results, we did not include this variable in the multivariable models given the high potential for bias. Last, mothers who smoke during pregnancy continue to smoke after delivery and it is difficult to distinguish between environmental exposure to smoke in utero or ex utero. Nonetheless, these smoking data provide more evidence to continue to encourage smoking cessation.

CONCLUSIONS

In summary, on the basis of these prospective, multicenter, multiyear data of children hospitalized with bronchiolitis, we found for the first time that in utero smoke exposure is independently associated with a subsequent need for CPAP and/or intubation. The present data not only build on and extend previous findings about the respiratory ramifications of in utero smoke exposure for infants, but they also emphasize the need for continued work on smoking cessation. In addition to the

demographic, historical, and clinical variables that predicted the need for mechanical respiratory support, we found a novel subgroup of children with bronchiolitis that have a rapid respiratory decline. Although this large study has clarified the characteristics of the children who have the most severe bronchiolitis, the next steps are to examine why and how these children differ from the majority of children who do not require mechanical respiratory support. As bronchiolitis research moves forward, the subgroup of children with rapid respiratory decline will be of particular interest and may yield important insights for the future management of children with bronchiolitis.

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TABLE 3 Multivariable Predictors of Receiving Inpatient CPAP and/or Intubation Among Children With Bronchiolitis

Characteristics	OR	BCa 95% CI
Age in months		
<2	4.29	1.66–11.53
2–5.9	2.61	1.16–6.10
6–11.9	1.59	0.68–4.94
≥12	1.00	(reference)
Gender		
Male	1.00	(reference)
Female	0.86	0.56–1.40
Race		
White	1.00	(reference)
Black	0.66	0.31–1.21
Other or missing	1.44	0.57–2.97
Birth weight, pounds		
<5	1.70	1.01–2.52
≥5	1.68	1.03–2.68
≥7	1.00	(reference)
Smoked during pregnancy	1.38	1.05–1.91
When difficulty breathing began (preadmission)		
≥1 d	1.00	(reference)
<1 d	1.58	1.15–2.09
No difficulty preadmission	0.59	0.12–3.41
Presence of apnea (chart)	4.78	2.57–8.50
Retractions		
None	1.00	(reference)
Mild	0.83	0.45–1.68
Moderate	2.36	0.77–5.38
Severe	11.14	2.40–33.19
Missing	1.78	0.27–4.55
Oxygen saturation by pulse oximeter or ABG		
<85	3.28	2.02–4.82
85–87.9	1.34	0.57–3.43
88–89.9	1.91	0.79–3.80
90–93.9	1.15	0.70–1.52
≥94	1.00	(reference)
Oral intake		
Adequate	1.00	(reference)
Inadequate	2.51	1.34–4.26
Missing	2.47	1.34–5.07

BCa 95% CI, bias-corrected and accelerated 95% confidence intervals; ABG, arterial blood gas.

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This study was supported by the grants U01 AI-67693 and K23 AI-77801 from the National Institutes of Health (Bethesda, MD). The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Allergy and Infectious Diseases or the National Institutes of Health. Funded by the National Institutes of Health (NIH).