RESEARCH ARTICLE

Risk Factors for Respiratory Decompensation Among Healthy Infants With Bronchiolitis

Nina M. Dadlez, MD, MS,[a,b] Nora Esteban-Cruciani, MD, MS,[c,d] Asama Khan, BA,[b] Lindsey C. Douglas, MD, MS,[a,b] Yi Shi, MD,[e] William N. Southern, MD, MS[f,g]

ABSTRACT

BACKGROUND: Although most children with bronchiolitis only require supportive care, some decompensate and require ventilatory support. We examined predictors of respiratory decompensation among hospitalized children to identify which patients may benefit from expectant monitoring.

METHODS: We examined children ≤24 months old with bronchiolitis admitted to the general infant and toddler floor. Children with pneumonia or comorbidities were excluded. Demographic and clinical characteristics were abstracted from a clinical database and medical records. Respiratory decompensation was defined as the need for initiating high-flow nasal cannula oxygen, continuous positive airway pressure, nasal intermittent mandatory ventilation, bilevel positive airway pressure, or intubation. A multivariable logistic regression model was constructed to identify independent predictors of respiratory decompensation.

RESULTS: A total of 1217 children were included. The median age was 6.9 months, 41% were girls, 49% were Hispanic, 21% were black, and 18% were premature. Significant independent predictors of respiratory decompensation were age ≤3 months (odds ratio [OR]: 3.25; 95% confidence interval [CI]: 2.09–5.07), age 3 to 6 months (OR: 1.76; 95% CI: 1.04–3.0), black race (OR: 1.94; 95% CI: 1.27–2.95), emergency department hypoxemia (OR: 2.34; 95% CI: 1.30–4.21), and retractions or accessory muscle use (OR: 2.26; 95% CI: 1.48–3.46). Children with 0 of 4 predictors were found to have a low risk of decompensation (3%).

CONCLUSIONS: Young age, black race, emergency department hypoxemia, and retractions or accessory muscle use were associated with respiratory decompensation in children with bronchiolitis. These factors should be considered at presentation, as they identify children who require a higher level of respiratory monitoring and support and others who may not benefit.

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2017-0034

Address correspondence to Nina M. Dadlez, MD, MS, Department of Pediatrics, The Children's Hospital at Montefiore, 3411 Wayne Ave, Bronx, NY 10467. E-mail: ndadlez@montefiore.org

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

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

FUNDING: The research described was supported by the National Institutes of Health/National Center for Advancing Translational Science (NCATS) Einstein-Montefiore CTSA Grant UL1TR001073. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Dr Dadlez conceptualized and designed the study, collected data, conducted the analyses, and drafted the manuscript; Dr Esteban-Cruciani and Dr Douglas conceptualized and designed the study, reviewed analyses, and reviewed and revised the manuscript; Mr Khan and Dr Shi collected data, reviewed the analyzed data, and reviewed and revised the manuscript; Dr Southern conceptualized and designed the study, reviewed the analytic plan and analyses, and critically revised the manuscript; and all authors approved the final manuscript as submitted.

[a]Division of Pediatric Hospital Medicine, Department of Pediatrics, The Children's Hospital at Montefiore, New York, New York; [f]Division of Hospital Medicine, Department of Medicine and [b]Department of Pediatrics, Albert Einstein College of Medicine, New York, New York; [c]Department of Pediatrics, St Christopher's Hospital for Children, Philadelphia, Pennsylvania; [d]Einstein Medical Center Philadelphia, Pennsylvania; [e]Department of Pediatrics, Jacobi Medical Center, New York, New York; and [g]Department of Medicine, Montefiore Medical Center, New York, New York

Viral bronchiolitis is an acute infectious inflammatory condition of the airways, which causes significant respiratory distress in infants and young children. Bronchiolitis represents a substantial public health burden in the United States, accounting for 16% of hospitalizations of children <2 years of age and over $1.73 billion in hospital charges annually.[1] Although most children require only supportive care, ~2% to 7% decompensate and develop respiratory failure requiring ventilatory support.[2–4] These events can be particularly dangerous if the patient is cared for at a hospital that does not have a pediatric ICU. In bronchiolitis, studies have revealed that the nonselective use of monitoring including pulse oximetry can lead to worse outcomes such as prolonged length of stay and may be unnecessary for many children.[5–7] Identification of risk factors for decompensation would enable clinicians to selectively determine which children are at higher risk and may benefit from expectant monitoring and which children are lower risk and would not benefit from additional surveillance.

Although some studies have examined predictors of the development of hypoxemia or need for ICU management among children with bronchiolitis, few focused on otherwise healthy children admitted to the general floor.[2,6–13] In addition, because of small sample sizes, many of these studies had a low event rate and were not appropriately powered to identify meaningful associations of risk factors with respiratory decompensation.[5] The ability to identify high- and low-risk cohorts of infants with bronchiolitis would aid in triage and resource utilization decisions, both in academic and community settings.

To address this gap, we sought to identify early predictors of respiratory decompensation among otherwise healthy children with bronchiolitis admitted to the general infant and toddler floor. We hypothesized that demographic and clinical factors identifiable on presentation to the emergency department (ED) would be associated with subsequent decompensation and need for ventilatory support and that evaluation of risk factors would identify high- and low-risk populations who would or would not benefit from expectant monitoring.

METHODS

Study Population

Children 24 months or younger admitted with a primary or secondary diagnosis of bronchiolitis to the general pediatric infant and toddler unit through the ED at an urban tertiary care center over a 4-year period from April 1, 2011, to March 31, 2015, were identified by using *International Classification of Diseases, Ninth Revision* codes 466.11 and 466.19. Children who required ventilatory support at the time of presentation to the ED and children who were not evaluated in the ED were excluded. Risk factors for respiratory decompensation may be different for children with a concomitant pneumonia; therefore, children diagnosed with pneumonia by a hospital medicine attending physician and treated with antibiotics were excluded from the study. In addition, risk factors for respiratory decompensation are likely also different for children with complex comorbidities that impact respiratory status. Therefore, to identify a cohort of otherwise healthy children, by using the method described by Ralston et al,[14] children with chronic illness (cardiac, pulmonary, neurologic, chromosomal, or craniofacial comorbidities) were also excluded. Patients were excluded by using *International Classification of Diseases, Ninth Revision* codes, and exclusions were verified by manual chart review; this methodology was reviewed by 2 study investigators to ensure accuracy.

Data Collection

Demographic and admission characteristics were abstracted from Montefiore's Clinical Information System by using the Clinical Looking Glass tool.[15] Patient clinical history and clinical findings, including medical history, family history, vital signs, and physical examination findings were obtained through review of electronic medical records. Ten percent of all records were examined by a second reviewer to ensure accuracy. This study was approved by the institutional review board at Montefiore Medical Center.

Outcome Measure and Predictor Variables

The primary outcome measure was respiratory decompensation as evidenced by the addition of ventilatory support, which included the need for high-flow nasal cannula, continuous positive airway pressure, nasal intermittent mandatory ventilation, or bilevel positive airway pressure or intubation. Candidate predictor variables were selected a priori on the basis of clinical significance and literature review and included demographic characteristics, clinical history, and clinical findings. Demographic characteristics included age, sex, insurance, and race and/or ethnicity. Age at admission was examined as a continuous variable in bivariable analysis and coded as age <3 months and age 3 to 6 months for multivariable analysis based on threshold effects noted on locally weighted scatterplot smoothing curves. Race and/or ethnicity was categorized as black, Hispanic, white, or other or unknown. Clinical history variables included history of prematurity (<37 weeks' gestational age), previous respiratory admission, previous ICU admission, and first-degree relative with asthma. Previous respiratory admission, previous ICU admission, and first-degree relative with asthma were all categorized as yes or no. Clinical findings variables included weight-for-age *z* score, hypoxemia in the ED, peak respiratory rate in the ED, and retractions or accessory muscle use on the ED physical examination. Weight-for-age *z* scores derived from admission weight according to the World Health Organization criteria and corrected for gestational age were obtained utilizing the egen zanthro package published by Vidmar et al.[16] Hypoxemia was defined as an oxygen saturation of <90% on pulse oximetry.

Statistical Analysis

To assess the unadjusted associations of demographic and clinical characteristics with respiratory decompensation, χ^2 tests, Fisher's exact tests, *t* tests, and Wilcoxon rank sum tests were performed.

A multivariate logistic regression model was then constructed to identify independent predictors of respiratory decompensation, with the independent variables (demographic, clinical history, and clinical findings) as candidates for inclusion. First, continuous variables were assessed for linearity in the logit and threshold effects utilizing locally weighted scatterplot smoothing curves, and specified appropriately. Next, a full logistic regression model was constructed to include all candidate variables. Variables were assessed for collinearity and all had a variance inflation factor <2. A backward stepwise regression was performed to create a parsimonious model (removal criterion $P \geq .05$). Then, first-order interactions were assessed for variables thought to have a potential interaction on the basis of clinical plausibility and theory (eg, age and respiratory rate). Finally, the C-statistics for the full model and each parsimonious model were compared with model fit and discriminative potential.

By using the parsimonious multivariate model described above, a composite score of risk was created. By using the coefficients derived in the predictive model, an index of risk for respiratory decompensation, the Bronchiolitis Risk Score, was calculated for each patient (Supplemental Information). To test the calibration of the composite score, the cohort was divided into predicted risk quartiles, and for each quartile, the observed and predicted risks of respiratory decompensation were compared. All analyses were performed by using Stata 13.0 (StataCorp LLC, College Station, TX).

RESULTS

Study Population

During the 4 years of this study, 1611 children were admitted to the general infant and toddler unit at the Children's Hospital at Montefiore with a diagnosis of bronchiolitis. Of those, 90 children were excluded for concomitant pneumonia, 250 were excluded for comorbidities, and 54 were excluded because they were not evaluated in the ED. Therefore, 1217 children were included in the final analysis (Table 1). The median age was 6.9 months (interquartile range [IQR]: 2.7–12.9). Female children accounted for 41.4% of the cohort. The majority were Hispanic (48.6%) or black (20.8%), and they were primarily Medicaid recipients (82.1%). Premature infants accounted for 18.0% of the cohort. The majority of premature infants (80.7%) were late preterm (≥32 weeks' gestational age) with a median gestational age at birth among premature infants of 34 weeks (IQR: 32–36 weeks). Approximately one-fifth of the patients had a previous respiratory admission (21.0%).

TABLE 1 Participant Characteristics ($N = 1217$)

Characteristics	Number
Female (%)	504 (41.4)
Age, mo (median, IQR)	6.9 (2.7–12.9)
Race and/or ethnicity (%)	
Hispanic	592 (48.6)
Black	253 (20.8)
White	56 (4.6)
Other or unknown	316 (26.0)
Medicaid (%)	999 (82.1)
Premature (%)	219 (18.0)
Previous respiratory admission (%)	256 (21.0)
Previous respiratory ICU admission (%)	42 (3.5)

Respiratory Decompensation

Of the 1217 children included in the analysis, 121 (9.9%) had respiratory decompensation. The majority of children with respiratory decompensation were managed with noninvasive ventilation alone, and 1 child further decompensated and required intubation (Table 2).

In bivariable analyses, young age, black race, hypoxemia, peak respiratory rate on presentation to the ED, and retractions or accessory muscle use on presentation to the ED were significantly associated with respiratory decompensation during admission (Table 3). In addition, a larger fraction of children who had respiratory decompensation were premature (24.0% vs 17.0%), but the difference was not statistically significant ($P = .07$). Sex, a history of previous respiratory admission, Hispanic versus non-Hispanic ethnicity or white versus non-white race, and having a first-degree relative with asthma were not significantly associated with respiratory decompensation. Neither weight-for-age z score nor having a z score indicative of malnutrition (<-2) was significantly associated with respiratory decompensation.

In multivariable analyses, age <3 months (odds ratio [OR]: 3.25; 95% confidence interval [CI]: 2.09–5.07) and age 3 to 6 months (OR: 1.76; 95% CI: 1.04–3.00) were significantly and independently associated with respiratory decompensation when compared with a reference group of children older than 6 months (Table 4). In addition, black race (OR: 1.94; 95% CI: 1.27–2.95) was associated with respiratory decompensation when compared with non-black children. Finally, hypoxemia (OR: 2.34; 95% CI: 1.30–4.21) and retractions or accessory muscle use on presentation in the ED (OR: 2.26; 95% CI: 1.48–3.46) remained significantly associated with respiratory decompensation in

TABLE 2 Highest Level of Respiratory Support ($n = 121$)

Respiratory Support	No. (%)[a]
HFNC	88 (73)
CPAP	11 (9)
NIMV	18 (15)
BiPAP	3 (3)
Intubation	1 (1)

BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula; NIMV, nasal intermittent mandatory ventilation.

[a] Percentages do not add up to 100 because of rounding.

TABLE 3 Bivariable Associations With Respiratory Decompensation

Characteristics	Respiratory Failure (N = 1217)		P
	No (n = 1096)	Yes (n = 121)	
Age, mo (median, IQR)	7.2 (2.8–13.0)	4.2 (2.1–9.7)	.007
Female (%)	451 (41.2)	53 (43.8)	.57
Hispanic (%)	541 (49.4)	51 (42.4)	.13
Black (%)	215 (19.6)	38 (31.4)	.002
White (%)	50 (4.7)	6 (5.0)	.82
Prematurity (%)	190 (17.0)	29 (24.0)	.07
Previous respiratory admission (%)	234 (21.4)	22 (18.2)	.42
Previous respiratory ICU admission (%)[a]	36 (3.2)	6 (5.0)	.29
First degree relative with asthma (%)	505 (46.1)	57 (47.1)	.83
Weight-for-age z score (mean, SD)	0.1 (1.1)	0.1 (1.1)	.98
ED hypoxemia (%)	86 (7.9)	17 (14.0)	.02
ED peak respiratory rate in breaths per min (median, IQR)	54 (48–62)	58 (52–64)	.002
ED respiratory distress (%)	588 (53.7)	85 (70.3)	<.001

[a] Fisher's exact tests were used.

multivariable analysis. Sex, Hispanic race, prematurity, a history of a previous respiratory admission, weight-for-age z score, and peak respiratory rate in the ED were not significantly associated with respiratory decompensation. The final model had a C-statistic of 0.70 for predicting respiratory decompensation. Of the 190 children who had none of the independent risk factors, only 3% (n = 6) had respiratory decompensation.

Composite Score and Calibration

A composite score of risk, the Bronchiolitis Risk Score, was calculated for each patient. (Supplemental Information) The median Bronchiolitis Risk Score was 1.18 (range: 0–3.51; IQR: 0.66–1.48). Each increase in the Bronchiolitis Risk Score of 1 was associated with a 2.7 increased odds of respiratory decompensation. The model was an accurate predictor of respiratory decompensation across all quartiles of risk (Fig 1).

TABLE 4 Multivariable Associations With Respiratory Decompensation (N = 1217)

Independent Variable	OR	95% CI	P
Age ≤3 mo	3.25	2.09–5.07	<.001
Age 3–6 mo	1.76	1.04–3.00	.04
Black race	1.94	1.27–2.95	.002
ED hypoxemia	2.34	1.30–4.21	.005
ED respiratory distress	2.26	1.48–3.46	<.001

DISCUSSION

We found that age <3 months, age 3 to 6 months, black race, hypoxemia, and retractions or accessory muscle use on presentation in the ED are independent predictors of respiratory decompensation as evidenced by the need for ventilatory support. Our findings revealed that infants in the highest risk quartile had ~20% risk of respiratory decompensation, indicating that there is a high-risk group of otherwise healthy infants with bronchiolitis that would likely benefit from expectant monitoring for decompensation. In addition, we found that infants with none of these characteristics had a low risk of respiratory decompensation (3%) and therefore may not benefit from higher levels of care, which may have important implications in terms of the safety of managing this group in a low-resource environment.

Several of the specific factors we examined are worth noting, including age, black race, hypoxemia on presentation in the ED, and retractions or accessory muscle use on presentation in the ED. First, we found that young age (<6 months) was a significant predictor of respiratory decompensation. Furthermore, there was an incremental increased risk of respiratory decompensation in the youngest children (<3 months). Although this is consistent with previous studies revealing that infants <2 months old are at-risk for decompensation, we found that the increased risk of respiratory decompensation extends to children up to 6 months of age.[10,11] Next, we found a higher risk of respiratory decompensation among children of black race. Research on the severity of bronchiolitis among black children is inconsistent. In 1 study, black children had higher oxygen saturations during admission and shorter lengths of stay than their white counterparts.[17] However, the authors of multiple studies have found an increased risk of mortality among black children with bronchiolitis when compared with white children.[18–20] The etiology of worse outcomes among black patients in our study population is unclear and may represent the influence of unmeasured environmental factors and disparities in health care. In addition, our results must also be interpreted with caution, given the large proportion of patients who were coded as "other or unknown" race (26.0%). Finally, of the clinical factors examined, hypoxemia on presentation to the ED and retractions or accessory muscle use on presentation to the ED were each associated with a twofold greater increased risk of developing subsequent respiratory decompensation. Although 1 study revealed that smaller reductions in oxygen saturations were not associated with worse outcomes, we found that more profound hypoxemia on presentation to the ED with a saturation of <90% was an independent risk factor for respiratory decompensation after admission.[21]

Previous research has revealed that the nonselective use of continuous pulse oximetry in bronchiolitis can lead to a prolonged length of stay and may be unnecessary for many children.[5,7] We found that children who have none of the risk factors identified (age <6 months, black race, hypoxemia on presentation to the ED, or retractions or accessory

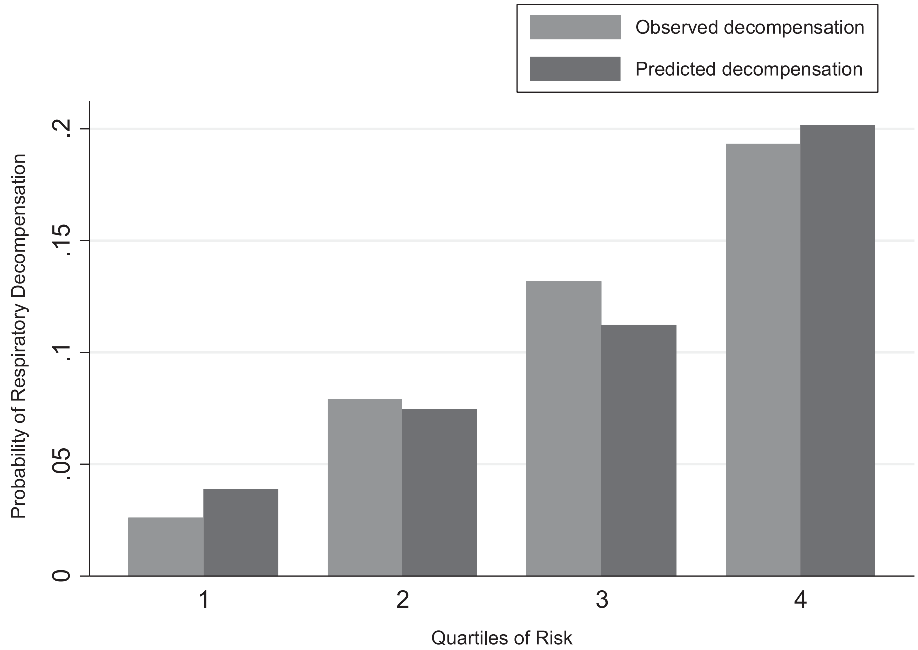

FIGURE 1 Observed versus predicted respiratory decompensation by quartiles of risk.

muscle use on presentation to the ED) have a low risk of respiratory decompensation and may not benefit from higher levels of monitoring. This may indicate that these infants can be managed in a lower resource environment. However, our findings do suggest that there may be a cohort of patients at higher risk for respiratory decompensation during the course of their admission who may benefit from expectant monitoring on the general pediatric floor. This monitoring for patients with high-risk characteristics may include more frequent respiratory checks and vital sign review, heightened awareness of potential to decompensate, and, for patients managed in a community hospital setting, consideration of early transfer to a tertiary care facility. Further research is needed to establish if expectant monitoring for high-risk subsets can improve outcomes in this population and if we can safely do less for lower-risk subsets.

One of the factors that we did not find to be associated with respiratory decompensation is also worth noting. Researchers have shown a history of prematurity to be associated with increased severity of bronchiolitis.[3,22] Additionally, some researchers have found that a birth weight <5 pounds, which may identify premature infants, is associated with severe bronchiolitis.[9,10] We did not find a significant association between prematurity and the risk of respiratory decompensation; however, this is likely because of the fact that we excluded children with comorbidities. In removing children with chronic lung disease from our population, we excluded the majority of early preterm infants. In addition, given the low number of preterm children in our sample (24), we may have been underpowered to detect the associated risk for decompensation.

Our study has several limitations. It is a single-institution study at an urban tertiary care center with a high proportion of minorities, and our inferences therefore may not be generalizable to other clinical settings. In addition, our outcome of interest, respiratory decompensation, could not be directly measured; therefore, we assessed associations with need for ventilatory support as a surrogate. Because our study was observational in nature, there may be additional predictors that we were unable to measure, such as tobacco smoke exposure or day of illness of bronchiolitis course. In addition, we were limited by the variables available in the medical record and in our electronic clinical information system. Finally, because of limitations with our data, we were not able to accurately measure the time from admission to respiratory decompensation and were consequently unable to perform a time-to-event analysis.

CONCLUSIONS

We found that age <6 months, black race, hypoxemia in the ED, and retractions or accessory muscle use on ED physical examination are independent predictors of respiratory decompensation after admission among otherwise healthy children with bronchiolitis admitted initially to the general floor. We believe that these factors should be considered by clinicians in determining which children selectively require a higher level of monitoring, or require transfer to another institution if the appropriate monitored setting is not available or if the capability to provide ventilatory support is limited.

REFERENCES

1. Healthcare Cost and Utilization Project; Agency for Healthcare Research and Quality. HCUP Kids' Inpatient Database (KID). Available at: www.hcup-us.ahrq.gov/kidoverview.jsp. Accessed November 11, 2015

2. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA Jr. Trends in bronchiolitis hospitalizations in the United States, 2000-2009. *Pediatrics*. 2013;132(1):28–36

3. Chan PW, Lok FY, Khatijah SB. Risk factors for hypoxemia and respiratory failure in respiratory syncytial virus bronchiolitis. *Southeast Asian J Trop Med Public Health*. 2002;33(4):806–810

4. Outwater KM, Crone RK. Management of respiratory failure in infants with acute viral bronchiolitis. *Am J Dis Child*. 1984;138(11):1071–1075

5. American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics*. 2006;118(4):1774–1793

6. Ralston SL, Lieberthal AS, Meissner HC, et al; American Academy of Pediatrics. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics*. 2014;134(5). Available at: www.pediatrics.org/cgi/content/full/134/5/e1474

7. McCallum GB, Chatfield MD, Morris PS, Chang AB. Risk factors for adverse outcomes of indigenous infants hospitalized with bronchiolitis. *Pediatr Pulmonol*. 2016;51(6):613–623

8. Hasegawa K, Pate BM, Mansbach JM, et al. Risk factors for requiring intensive care among children admitted to ward with bronchiolitis. *Acad Pediatr*. 2015;15(1):77–81

9. Mansbach JM, Piedra PA, Stevenson MD, et al; MARC-30 Investigators. Prospective multicenter study of children with bronchiolitis requiring mechanical ventilation. *Pediatrics*. 2012;130(3). Available at: www.pediatrics.org/cgi/content/full/130/3/e492

10. Damore D, Mansbach JM, Clark S, Ramundo M, Camargo CA Jr. Prospective multicenter bronchiolitis study: predicting intensive care unit admissions. *Acad Emerg Med*. 2008;15(10):887–894

11. Brooks AM, McBride JT, McConnochie KM, Aviram M, Long C, Hall CB. Predicting deterioration in previously healthy infants hospitalized with respiratory syncytial virus infection. *Pediatrics*. 1999;104(3, pt 1):463–467

12. Wang EE, Law BJ, Stephens D. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr*. 1995;126(2):212–219

13. Schroeder AR, Marmor AK, Pantell RH, Newman TB. Impact of pulse oximetry and oxygen therapy on length of stay in bronchiolitis hospitalizations. *Arch Pediatr Adolesc Med*. 2004;158(6):527–530

14. Ralston S, Garber M, Narang S, et al. Decreasing unnecessary utilization in acute bronchiolitis care: results from the value in inpatient pediatrics network. *J Hosp Med*. 2013;8(1):25–30

15. *Clinical Looking Glass* [computer program]. New York, NY: Emerging Health Information Technology; 2009

16. Vidmar SI, Cole TJ, Pan H. Standardizing anthropometric measures in children and adolescents with functions for egen: update. *Stata J*. 2013;13(2):366–378

17. Bradley JP, Bacharier LB, Bonfiglio J, et al. Severity of respiratory syncytial virus bronchiolitis is affected by cigarette smoke exposure and atopy. *Pediatrics*. 2005;115(1). Available at: www.pediatrics.org/cgi/content/full/115/1/e7

18. Holman RC, Shay DK, Curns AT, Lingappa JR, Anderson LJ. Risk factors for bronchiolitis-associated deaths among infants in the United States. *Pediatr Infect Dis J*. 2003;22(6):483–490

19. Shay DK, Holman RC, Roosevelt GE, Clarke MJ, Anderson LJ. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979-1997. *J Infect Dis*. 2001;183(1):16–22

20. Leader S, Kohlhase K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. *J Pediatr*. 2003;143(suppl 5):S127–S132

21. Schuh S, Freedman S, Coates A, et al. Effect of oximetry on hospitalization in bronchiolitis: a randomized clinical trial. *JAMA*. 2014;312(7):712–718

22. Sala KA, Moore A, Desai S, Welch K, Bhandari S, Carroll CL. Factors associated with disease severity in children with bronchiolitis. *J Asthma*. 2015;52(3):268–272