ORIGINAL RESEARCH

Hospital Course and Discharge Criteria for Children Hospitalized With Bronchiolitis

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BACKGROUND: For children hospitalized with bronchiolitis, there is uncertainty about the expected inpatient clinical course and when children are safe for discharge.

OBJECTIVES: Examine the time to clinical improvement, risk of clinical worsening after improvement, and develop discharge criteria.

DESIGN: Prospective multiyear cohort study.

SETTING: Sixteen US hospitals.

PARTICIPANTS: Consecutive hospitalized children age <2 years with bronchiolitis.

MEASUREMENT: We defined clinical improvement using: (1) retraction severity, (2) respiratory rate, (3) room air oxygen saturation, and (4) hydration status. After meeting improvement criteria, children were considered clinically worse based on the inverse of ≥ 1 of these criteria or need for intensive care.

RESULTS: Among 1916 children, the median number of days from onset of difficulty breathing until clinical improve-

ment was 4 (interquartile range, 3–7.5 days). Of the total, 1702 (88%) met clinical improvement criteria, with 4% worsening (3% required intensive care). Children who worsened were age <2 months (adjusted odds ratio [AOR]: 3.51; 95% confidence interval [CI]: 2.07-5.94), gestational age <37 weeks (AOR: 1.94; 95% CI: 1.13-3.32), and presented with severe retractions (AOR: 5.55; 95% CI: 2.12-14.50), inadequate oral intake (AOR: 2.54; 95% CI: 1.39-4.62), or apnea (AOR: 2.87; 95% CI: 1.45-5.68). Readmissions were similar for children who did and did not worsen.

CONCLUSIONS: Although children hospitalized with bronchiolitis had wide-ranging recovery times, only 4% worsened after initial improvement. Children who worsened were more likely to be younger, premature infants presenting in more severe distress. For children hospitalized with bronchiolitis, these data may help establish more evidence-based discharge criteria, reduce practice variability, and safely shorten hospital length-of-stay. *Journal of Hospital Medicine* 2015;10:205–211. © 2015 Society of Hospital Medicine

Although bronchiolitis is the leading cause of hospitalization for US infants, there is a lack of basic prospective data about the expected inpatient clinical course and ongoing uncertainty about when a hospitalized child is ready for discharge to home. This lack of data about children's readiness for discharge may result in variable hospital length-of-stay (LOS). The state of th

One specific source of variability in discharge readiness and LOS variability may be the lack of consensus about safe threshold oxygen saturation values for discharge in children hospitalized with bronchiolitis.^{6,7} In 2006, the Scottish Intercollegiate Guidelines Net-

work recommended a discharge room air oxygen (RAO2) saturation threshold of $\geq 95\%$. The same year, the American Academy of Pediatrics (AAP) bronchiolitis clinical practice guideline stated that oxygen is not needed for children with RAO2 saturations $\geq 90\%$ who are feeding well and have minimal respiratory distress. There is a need for prospective studies to help clinicians make evidenced-based discharge decisions for this common condition.

We performed a prospective, multicenter, multiyear study^{10–12} to examine the typical inpatient clinical course of and to develop hospital discharge guidelines for children age <2 years hospitalized with bronchiolitis. We hypothesized that children would not worsen clinically and would be safe to discharge home once their respiratory status improved and they were able to remain hydrated.

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Additional Supporting Information may be found in the online version of this article.

Received: October 1, 2014; Revised: November 12, 2014; Accepted: November 14, 2014

2015 Society of Hospital Medicine DOI 10.1002/jhm.2318 Published online in Wiley Online Library (Wileyonlinelibrary.com).

METHODS

Study Design and Population

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 in year 1, 16 in year 2, and 14 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 intensive care unit (ICU). We aimed to enroll 20% of our total sample from the ICU. To over sample children in the ICU, the ward and ICU enrollments were separate. Once the site reached their 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. Therefore, children with comorbid conditions were included in this study. All consent and data forms were translated into Spanish. The institutional review board at each of the 16 participating hospitals approved the study.

Of the 2207 enrolled children, we excluded 109 (5%) children with a hospital LOS <1 day due to inadequate time to capture the required data for the present analysis. Among the 2098 remaining children, 1916 (91%) had daily inpatient data on all factors used to define clinical improvement and clinical worsening. Thus, the analytic cohort was comprised of 1916 children hospitalized for bronchiolitis.

Data Collection

Investigators conducted detailed structured interviews. Chart reviews were conducted to obtain preadmission and daily hospital clinical data including respiratory rates, daily respiratory rate trends, degree of retractions, oxygen saturation, daily oxygen saturation trends, medical management, and disposition. These data were manually reviewed, and site investigators were queried about missing data and discrepancies. A follow-up telephone interview was conducted with families 1 week after discharge to examine relapse events at both 24 hours and 7 days.

We used the question: "How long ago did the following symptoms [eg, difficulty breathing] begin [for the] current illness?" to estimate the onset of the current illness. Pulse was categorized as low, normal, or high based on age-related heart rate values. ¹³ Presence of apnea was recorded daily by site investigators. ¹⁴

Nasopharyngeal Aspirate Collection and Virology Testing

As described previously, site teams used a standardized protocol to collect nasopharyngeal aspirates, 11 which were tested for respiratory syncytial virus (RSV) types A and B; rhinovirus (RV); 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, and adenovirus using polymerase chain reaction. ^{11,15–17}

Defining Clinical Improvement and Worsening

Clinical improvement criteria were based on the 2006 AAP guidelines.9 For respiratory rate and oxygen saturation, clinicians estimated average daily respiratory rate and oxygen saturation based on the recorded readings from the previous 24 hours. This estimation reflects the process clinicians use when rounding on their hospitalized patients, and thus may be more similar to standard clinical practice than a calculated mean. The respiratory rate criteria are adjusted for age. 18,19 For daily estimated average oxygen saturation we used the AAP criteria of RAO2 saturation of 90%. Considering that oxygen saturation is the main determinant of LOS,²⁰ healthy infants age <6 months may have transient oxygen saturations of around 80%,²¹ and that errors in estimation may occur, we included a lowest RAO2 of 88% in our improvement criteria. By combining the dichotomized estimated oxygen saturation (\geq 90% or not) with the lower limit of 88%, there was little room for erroneous conclusions. A child was considered clinically improved on the earliest date he/she met all of the following criteria: (1) none or mild retractions and improved or stable retractions compared with the previous inpatient day; (2) daily estimated average respiratory rate (RR) <60 breaths per minute for age <6 months, <55 breaths/minute for age 6 to 11 months, and <45 breaths/minute for age ≥12 months with a decreasing or stable trend over the course of the current day; (3) daily estimated average RAO2 saturation ≥90%, lowest RAO2 saturation ≥88%²¹; and (4) not receiving intravenous (IV) fluids or for children receiving IV fluids a clinician report of the child maintaining oral hydration. Children who reached the clinical improvement criteria were considered clinically worse if they required intensive care or had the inverse of ≥ 1 of the improvement criteria: moderate/severe retractions that were worse compared with the previous inpatient day, daily average RR >60 with an increasing trend over the current day, need for oxygen, or need for IV fluids.

Statistical Analyses

All analyses were performed using Stata 12.0 (Stata-Corp, College Station, TX). Data are presented as proportions with 95% confidence intervals (95% CIs), means with standard deviations, and medians with interquartile ranges (IQR). To examine potential factors associated with clinical worsening after reaching

clinical improvement, we used χ^2 , Fisher exact, Student t test, and Kruskall-Wallis tests, as appropriate.

Adjusted analyses used generalized linear mixed models with a logit link to identify independent risk factors for worsening after reaching clinical improvement. Fixed effects for patient-level factors and a random site effect were used. Factors were tested for inclusion in the multivariable model if they were found to be associated with worsening in unadjusted analyses (P < 0.20) or were considered clinically important. Results are reported as odds ratios with 95% CIs.

We performed several sensitivity analyses to evaluate these improvement criteria: (1) we excluded the lowest RAO2 saturation requirement of 88%, (2) we examined a 94% daily estimated average RAO2 saturation threshold, (3) we examined a 95% daily estimated average RAO2 saturation threshold, and (4) we examined children age <12 months with no history of wheeze.

RESULTS

There were 1916 children hospitalized with bronchiolitis with data on all factors used to define clinical improvement and clinical worsening. The median number of days from the beginning of difficulty breathing until admission was 2 days (IQR, 1–5.5 days; range, 1–8 days) and from the beginning of difficulty breathing until clinical improvement was 4 days (IQR, 3–7.5 days; range, 1–33 days) (Figure 1). The variance for days to admission was significantly less than the variance for days to clinical improvement (P < 0.001).

In this observational study, clinicians discharged 214 (11%) of the 1916 children before meeting the definition of clinical improvement. Thus, 1702 (89%; 95% CI: 87%-90%) children reached the clinical improvement criteria, had a LOS >1 day, and had data on all factors (Figure 2).

Of the 1702 children who met the clinical improvement criteria, there were 76 children (4%; 95% CI: 3%–5%) who worsened (Figure 2). The worsening

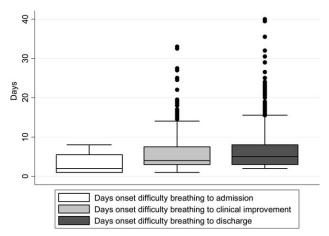


FIG. 1. Time course of illness for children hospitalized with bronchiolitis.

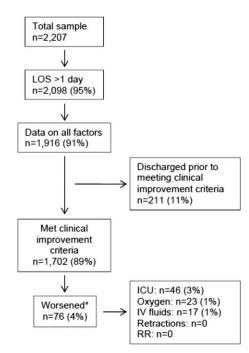


FIG. 2. Flow diagram of the study population. *Eight children were worsened on more than 1 criterion. Abbreviations: ICU, intensive care unit; IV, intravenous; LOS, length of stay; RR, respiratory rate.

occurred within a median of 1 day (IOR, 1-3 days) of clinical improvement. Forty-six (3%) of the children required transfer to the ICU (1 required intubation, 1 required continuous positive airway pressure, and 4 had apnea), 23 (1%) required oxygen, and 17 (1%) required IV fluids. Eight percent of children met multiple criteria for worsening. A comparison between children who did and did not worsen is shown in Table 1. In general, children who worsened after improvement were younger and born earlier. These children also presented in more severe respiratory distress, had moderate or severe retractions, oxygen saturation <85% at hospitalization, inadequate oral intake, and apnea documented during the hospitalization. Neither viral etiology nor site of care influenced whether the children worsened after improving. However, stratified analysis of children based on initial location of admission (ie, ICU or ward) showed that among the children admitted to the ICU from the emergency department (ED), 89% met the improvement criteria and 19% clinically worsened. In contrast, among children admitted to the ward from the ED, 89% met the improvement criteria, and only 2% clinically worsened. Stratified multivariable models based on the initial location of admission from the ED (ie, ICU or ward) were not possible due to small sample sizes after stratification. None of these children had relapse events requiring rehospitalization within either 24 hours or 7 days of discharge.

On multivariable analysis (Table 2), independent risk factors for worsening after reaching the clinical improvement criteria were young age, preterm birth, and presenting to care with more severe bronchiolitis

TABLE 1. Characteristics of Children Who Did Not Worsen Versus Those Who Worsened After Clinical Improvement

	Did Not Worsen,	Worsened,		
	n = 1,626	n = 76	P Value	
Demographic characteristics				
Age <2 months, %	29	57	< 0.001	
Month of birth, %	25	JI	0.001	
October–March	61	75	0.02	
April–September	39	75 25		
	39	20	0.51	
Sex, %	F0	FF	0.51	
Male	59	55 45		
Female	41	45	0.050	
Race, %	00	Ε0.	0.050	
White	63	58		
Black	23	34		
Other or missing	14	8	0.04	
Hispanic ethnicity, %	37	22	0.01	
Insurance, %			0.87	
Nonprivate	68	67		
Private	32	33		
Medical history				
Gestational age <37 weeks, %	23	39	0.002	
Birth weight, %			0.52	
<5 lbs	13	12		
\geq 5 lbs	34	41		
≥7 lbs	53	47		
Mother's age, median (IQR)	27 (23-33)	27 (22-33)	0.54	
Is or was breastfed, %	61	51	0.10	
Smoked during pregnancy, %	15	20	0.22	
Exposure to smoke, %	13	20	0.11	
Family history of asthma, %			0.89	
Neither parent	68	64		
Either mother or father	27	30		
Both parents	4	4		
Do not know/missing	2	1		
History of wheezing, %	23	17	0.24	
History of eczema, %	16	7	0.04	
History of intubation, %	9	12	0.50	
Major, relevant, comorbid	20	24	0.46	
medical disorder, %				
Current illness				
When difficulty breathing			0.63	
began, preadmission, %			0.00	
>1 day	70	75		
<1 day	28	23		
No difficulty preadmission	2	3		
Weight, lbs, median (IQR)	12.3 (8.8–17.4)	9.0 (6.6–13.2)	0.001	
Temperature, °F, median (IQR)	99.5 (98.6–100.6)	99.4 (98.1–100.4)	0.06	
	00.0 (00.0-100.0)	JJ.7 (JU.1-100.4)	0.00	
Pulse, beats per minute by age Low	0.3	Λ	0.02	
Normal	48	0 46		
High	51	54	0.00	
Respiratory rate, breaths	48 (40–60)	48 (38–64)	0.28	
per minute, median (IQR)			0.004	
Retractions, %	00	05	0.001	
None	22	25		
Mild	43	24		
Moderate	26	33		
Severe	4	12		
Missing	5	7		
Oxygen saturation by			0.001	
pulse oximetry or ABG, %				
<85	4	12		
85-87.9	3	4		
88-89.9	5	0		

TABLE 1. Continued

	Did Not Worsen, n = 1,626	Worsened, $n = 76$	P Value
>94	72	73	
Oral intake, %			< 0.001
Adequate	45	22	
Inadequate	42	63	
Missing	13	14	
Presence of apnea, %	7	24	< 0.001
RSV-A, %	44	41	0.54
RSV-B, %	30	25	0.36
HRV, %	24	24	0.88
Chest x-ray results during ED/preadmission visit			
Atelectasis	12	13	0.77
Infiltrate	13	11	0.50
Hyperinflated	18	21	0.47
Peribronchial cuffing/thickening	23	17	0.32
Normal	14	16	0.75
White blood count, median (IQR)	11.2 (8.7-14.4)	11.9 (9.2-14.4)	0.60
Platelet count, median (IQR)	395 (317-490)	430 (299-537)	0.56
Sodium, median (IQR)	138 (136-140)	137 (135-138)	0.19
Hospital length of stay, median (IQR) One-week follow-up	2 (1–4)	4.5 (2–8)	< 0.001
Relapse within 24 hours of hospital discharge requiring hospital admission, %	0.5	0	0.56
Relapse within 7 days of hospital discharge requiring hospital admission, %	1	0	0.35

NOTE: Abbreviations: ABG, arterial blood gas; ED, emergency department; HRV, human rhinovirus; IQR, interquartile range; RSV, respiratory syncytial virus.

represented by severe retractions, inadequate oral intake, or apnea. To further evaluate the improvement criteria in the current analysis, multiple sensitivity analyses were conducted. The frequency of clinical worsening after reaching the improvement criteria was stable when we examined different RA02 criteria in sensitivity analyses: (1) excluding RA02 as a criterion for improvement: 90% met improvement criteria and 4% experienced clinical worsening, (2) changing the average RA02 threshold for clinical improvement to 94%: 62% met improvement criteria and 6% experienced clinical worsening, and (3) changing the average RA02 threshold for clinical improvement to 95%: 47% met improvement criteria and 5% experienced clinical worsening. Furthermore, stratifying by age <2 months and restricting to more stringent definitions of bronchiolitis (ie, age <1 year or age <1 year + no history of wheezing) also did not materially change the results (see Supporting Figure 1 in the online version of this article).

We compared the 214 children who were discharged prior to reaching clinical improvement with the 1702 children who reached the clinical improvement criteria. The 214 children were less likely to be age <2 months (22% vs 30%; P=0.02). These 2 groups (214 vs 1702) were similar with respect to

TABLE 2. Multivariable Model of Factors Associated With a Worsening of Symptoms After Clinical Improvement.

	Odds Ratio	95% CI	P Value
Age <2 months	3.51	2.07-5.94	< 0.001
Gestational age <37 weeks	1.94	1.13-3.32	0.02
Retractions			
None	1.30	0.80-3.23	0.19
Mild	1.0	Reference	_
Moderate	1.91	0.99-3.71	0.06
Severe	5.55	2.12-14.50	< 0.001
Missing	1.70	0.53-5.42	0.37
Oral intake			
Adequate	1.00	Reference	_
Inadequate	2.54	1.39-4.62	0.002
Unknown/missing	1.88	0.79-4.44	0.15
Presence of apnea	2.87	1.45-5.68	0.003

NOTE: Abbreviations: CI, confidence interval.

severe retractions (2% vs 4%; P = 0.13), median respiratory rate (48 vs 48; P = 0.42), oxygen saturation <90% (15% vs 11%; P = 0.07), inadequate oral intake (50% vs 43%; P = 0.13), and rates of relapse events requiring rehospitalization within both 24 hours (0.6% vs 0.6%; P = 0.88) and 7 days (1% vs 1%; P = 0.90) of discharge.

DISCUSSION

In this large, multicenter, multiyear study of children hospitalized with bronchiolitis, we found that children present to a hospital in a relatively narrow time frame, but their time to recovery in the hospital is highly variable. Nonetheless, 96% of children continued to improve once they had: (1) improving or stable retractions rated as none/mild, (2) a decreasing or stable RR by age, (3) estimated average RAO2 saturation $\geq 90\%$ and lowest RAO2 saturation of 88%, and (4) were hydrated. The 4% of children who worsened after clinically improving were more likely to be age <2 months, born <37 weeks, and present with more severe distress (ie, severe retractions, inadequate oral intake, or apnea). Based on the low risk of worsening after clinical improvement, especially among children admitted to the regular ward (2%), we believe these 4 clinical criteria could be used as discharge criteria for this common pediatric illness with a predominantly monophasic clinical

Variability in hospital LOS for children with bronchiolitis exists in the United States³ and internationally. ^{4,5} Cheung and colleagues analyzed administrative data from over 75,000 children admitted for bronchiolitis in England between April 2007 and March 2010 and found sixfold variation in LOS between sites. They concluded that this LOS variability was due in part to providers' clinical decision making. ⁵ Srivastava and colleagues²³ addressed variable

clinician decision making in bronchiolitis and 10 other common pediatric conditions by embedding discharge criteria developed by expert consensus into admission order sets. They found that for children with bronchiolitis, the embedded discharge criteria reduced the median LOS from 1.91 to 1.87 days. In contrast to the single-center data presented by White and colleagues,²⁴ the prospective, multicenter MARC-30 data provide a clear understanding of the normal clinical course for children hospitalized with bronchiolitis, determine if children clinically worsen after clinical improvement, and provide data about discharge criteria for children hospitalized with bronchiolitis. Although there is a lack of rigorous published data, the lower tract symptoms of bronchiolitis (eg, cough, retractions) are said to peak on days 5 to 7 of illness and then gradually resolve. 25 In the present study, we found that the time from the onset of difficulty breathing until hospital admission is less variable than the time from the onset of difficulty breathing until either clinical improvement or discharge. Although 75% of children have clinically improved within 7.5 days of difficulty breathing based on the IQR results, the remaining 25% may have a more prolonged recovery in the hospital of up to 3 weeks. Interestingly, prolonged recovery times from bronchiolitis have also been noted in children presenting to the ED²⁶ and in an outpatient population.²⁷ It is unclear why 20% to 25% of children at different levels of severity of illness have prolonged recovery from bronchiolitis, but this group of children requires further investigation.

Given the variability of recovery times, clinicians may have difficulty knowing when a child is ready for hospital discharge. One of the main stumbling blocks for discharge readiness in children with bronchiolitis is the interpretation of the oxygen saturation value. 6,8,9,20,28 However, it should be considered that interpreting the oxygen saturation in a child who is clinically improving in the hospital setting is different than interpreting the oxygen saturation of a child in the ED or the clinic whose clinical course is less certain.²² In the hospital setting, using the oxygen saturation value in in the AAP guideline, 9 4% of children clinically worsened after they met the improvement criteria, a clinical pattern observed previously with supplemental oxygen.²⁸ This unpredictability may explain some of the variation in providers' clinical decision making.⁵ The children who worsened, and therefore deserve more cautious discharge planning, were young (<2 months), premature (<37 weeks gestational age), and presented in more severe distress. Those children admitted to the ICU from the ED worsened more commonly than children admitted to the ward (19% vs 2%). Interestingly, the viral etiology of the child's bronchiolitis did not influence whether a child worsened after reaching the improvement criteria. Therefore, although children with RV

bronchiolitis have a shorter hospital LOS than children with RSV bronchiolitis, ¹¹ the pattern of recovery did not differ by viral etiology.

In addition to unsafe discharges, clinicians may be concerned about the possibility of readmissions. Although somewhat controversial, hospital readmission is being used as a quality of care metric.^{29–31} One response to minimize readmissions would be for clinicians to observe children for longer than clinically indicated.³² However, shorter LOS is not necessarily associated with increased readmission rates.³³ Given that the geometric mean of hospital charges per child with bronchiolitis increased from \$6380 in 2000 to \$8530 in 2009,³⁴ the potential for safely reducing hospital LOS by using the discharge criteria proposed in the current study instead of other criteria⁸ may net substantial cost savings. Furthermore, reducing LOS would decrease the time children expose others to these respiratory viruses and possibly reduce medical errors.³⁵

Our study has some potential limitations. Because the study participants were all hospitalized, these data do not inform admission or discharge decisions from either the ED or the clinic; but other data address those clinical scenarios.²² Also, the 16 sites that participated in this study were large, urban teaching hospitals. Consequently, these results are not necessarily generalizable to smaller community hospitals. Although numerous data points were required to enter the analytic cohort, only 9% of the sample was excluded for missing data. There were 214 children who did not meet our improvement criteria by the time of discharge. Although the inability to include these children in the analysis may be seen as a limitation, this practice variability underscores the need for more data about discharging hospitalized children with bronchiolitis. Last, site teams reviewed medical records daily. More frequent recording of the clinical course would have yielded more granular data, but the current methodology replicates how data are generally presented during patient care rounds, when decisions about suitability for discharge are often considered.

CONCLUSION

We documented in this large multicenter study that most children hospitalized with bronchiolitis had a wide range of time to recovery, but the vast majority continued to improve once they reached the identified clinical criteria that predict a safe discharge to home. The children who worsened after clinical improvement were more likely to be younger, premature infants presenting in more severe distress. Although additional prospective validation of these hospital discharge criteria is warranted, these data may help clinicians make more evidence-based discharge decisions for a common pediatric illness with high practice variation, both in the United States³ and in other countries.^{4,5}

Acknowledgements

Collaborators in the MARC-30 Study: Besh Barcega, MD, Loma Linda University Children's Hospital, Loma Linda, CA; John Cheng, MD, Children's Healthcare of Atlanta at Egleston, Atlanta, GA; Dorothy Damore, MD, New York Presbyterian Hospital-Cornell, New York, NY; Carlos Delgado, MD, Children's Healthcare of Atlanta at Egleston, Atlanta, GA; Haitham Haddad, MD, Rainbow Babies & Children's Hospital, Cleveland, OH; Paul Hain, MD, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN; Frank LoVecchio, DO, Maricopa Medical Center, Phoenix, AZ; Charles Macias, MD MPH, Texas Children's Hospital, Houston, TX; Jonathan Mansbach, MD, MPH, Boston Children's Hospital, Boston, MA; Eugene Mowad, MD, Akron Children's Hospital, Akron, OH; Brian Pate, MD, Children's Mercy Hospital, Kansas City, MO; Mark Riederer, MD, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN; M. Jason Sanders, MD, Children's Memorial Hermann Hospital, Houston, TX; Alan R. Schroeder, MD, Santa Clara Valley Medical Center, San Jose, CA; Nikhil Shah, MD, New York Presbyterian Hospital-Cornell, New York, NY; Michelle Stevenson, MD, MS, Kosair Children's Hospital, Louisville, KY; Erin Stucky Fisher, MD, Rady Children's Hospital, San Diego, CA; Stephen Teach, MD, MPH, Children's National Medical Center, Washington, DC; Lisa Zaoutis, MD, Children's Hospital of Philadelphia, Philadelphia, PA.

Disclosures: This study was supported by 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. Drs. Mansbach and Piedra have provided consultation to Regeneron Pharmaceuticals. Otherwise, no authors report any potential conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

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