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Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis FREE

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This guideline is a revision of the clinical practice guideline, "Diagnosis and Management of Bronchiolitis," published by the American Academy of Pediatrics in 2006. The guideline applies to infants aged from 1 through 23 months of age. Other exclusions are noted. Each key

action statement indicates level of evidence, benefit-harm relationship, and level of recommendation. Key action statements are as follows:

Subjects: Infectious Diseases

Topics: bronchiolitis, cochrane collaboration, medline

Diagnosis

1a. Clinicians should diagnose bronchiolitis and assess disease severity on the basis of history and physical examination (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

1b. Clinicians should assess risk factors for severe disease, such as age less than 12 weeks, a history of prematurity, underlying cardiopulmonary disease, or immunodeficiency, when making decisions about evaluation and management of children with bronchiolitis (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

1c. When clinicians diagnose bronchiolitis on the basis of history and physical examination, radiographic or laboratory studies should not be obtained routinely (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Treatment

2. Clinicians should not administer albuterol (or salbutamol) to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

3. Clinicians should not administer epinephrine to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

4b. Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis (Evidence Quality: B; Recommendation Strength: Weak Recommendation [based on randomized controlled trials with inconsistent findings]).

5. Clinicians should not administer systemic corticosteroids to infants with a diagnosis of bronchiolitis in any setting (Evidence Quality: A; Recommendation Strength: Strong Recommendation).

6a. Clinicians may choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90% in infants and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength: Weak Recommendation [based on low level evidence and reasoning from first principles]).

6b. Clinicians may choose not to use continuous pulse oximetry for infants and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength: Weak Recommendation [based on low-level evidence and reasoning from first principles]).

7. Clinicians should not use chest physiotherapy for infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

8. Clinicians should not administer antibacterial medications to infants and children with a diagnosis of bronchiolitis unless there is a concomitant bacterial infection, or a strong suspicion of one (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

9. Clinicians should administer nasogastric or intravenous fluids for infants with a diagnosis of bronchiolitis who cannot maintain hydration orally (Evidence Quality: X; Recommendation Strength: Strong Recommendation).

Prevention

10a. Clinicians should not administer palivizumab to otherwise healthy infants with a

10b. Clinicians should administer palivizumab during the first year of life to infants with hemodynamically significant heart disease or chronic lung disease of prematurity defined as preterm infants <32 weeks 0 days' gestation who require >21% oxygen for at least the first 28 days of life (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

10c. Clinicians should administer a maximum 5 monthly doses (15 mg/kg/dose) of palivizumab during the respiratory syncytial virus season to infants who qualify for palivizumab in the first year of life (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

11a. All people should disinfect hands before and after direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

11b. All people should use alcohol-based rubs for hand decontamination when caring for children with bronchiolitis. When alcohol-based rubs are not available, individuals should wash their hands with soap and water (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

12a. Clinicians should inquire about the exposure of the infant or child to tobacco smoke when assessing infants and children for bronchiolitis (Evidence Quality: C; Recommendation Strength: Moderate Recommendation).

12b. Clinicians should counsel caregivers about exposing the infant or child to environmental tobacco smoke and smoking cessation when assessing a child for bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong).

13. Clinicians should encourage exclusive breastfeeding for at least 6 months to decrease the morbidity of respiratory infections. (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

14. Clinicians and nurses should educate personnel and family members on evidence-

Introduction

In October 2006, the American Academy of Pediatrics (AAP) published the clinical practice guideline "Diagnosis and Management of Bronchiolitis."[1] The guideline offered recommendations ranked according to level of evidence and the benefit-harm relationship. Since completion of the original evidence review in July 2004, a significant body of literature on bronchiolitis has been published. This update of the 2006 AAP bronchiolitis guideline evaluates published evidence, including that used in the 2006 guideline as well as evidence published since 2004. Key action statements (KASs) based on that evidence are provided.

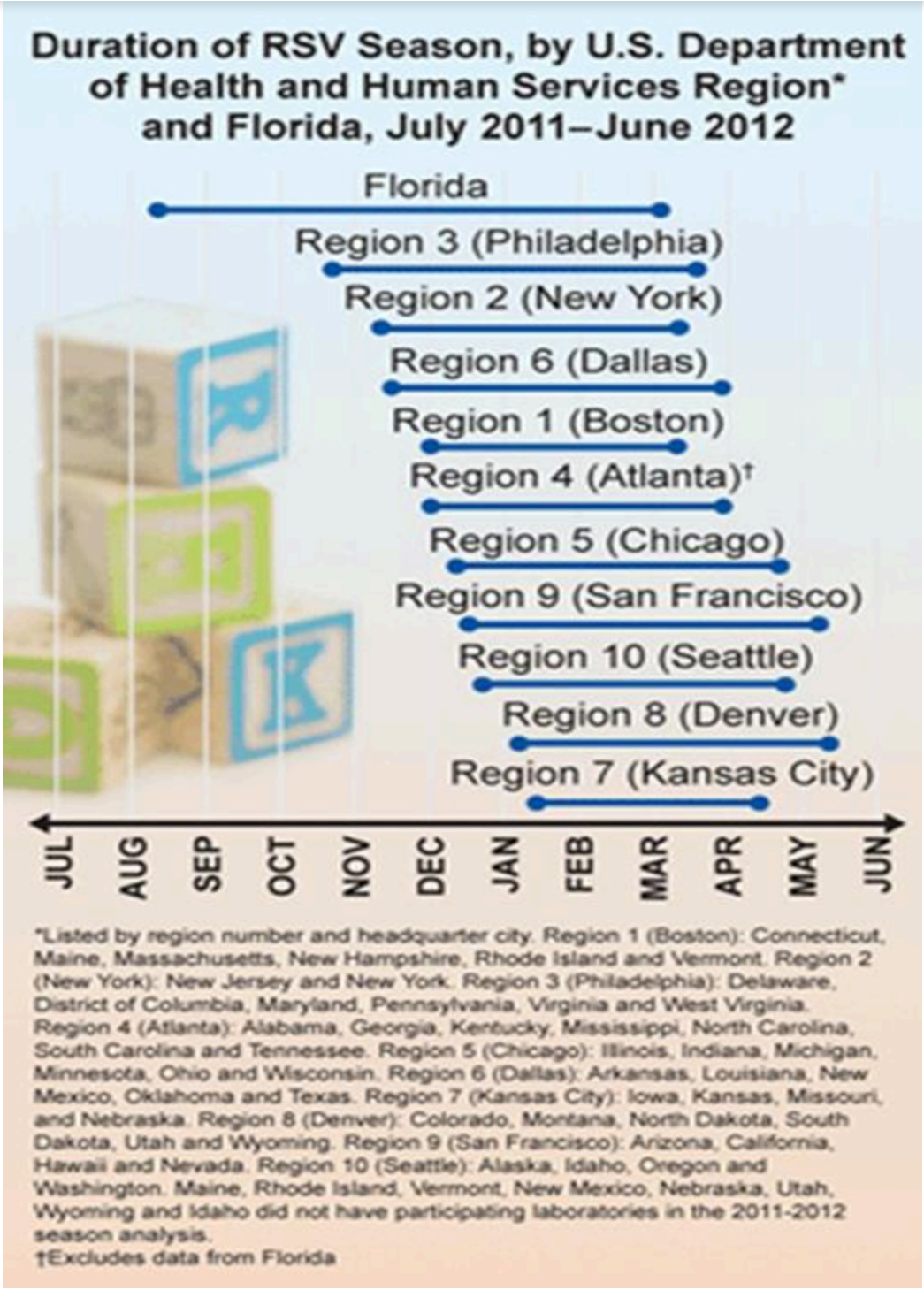
The goal of this guideline is to provide an evidence-based approach to the diagnosis, management, and prevention of bronchiolitis in children from 1 month through 23 months of age. The guideline is intended for pediatricians, family physicians, emergency medicine specialists, hospitalists, nurse practitioners, and physician assistants who care for these children. The guideline does not apply to children with immunodeficiencies, including those with HIV infection or recipients of solid organ or hematopoietic stem cell transplants. Children with underlying respiratory illnesses, such as recurrent wheezing, chronic neonatal lung disease (also known as bronchopulmonary dysplasia), neuromuscular disease, or cystic fibrosis and those with hemodynamically significant congenital heart disease are excluded from the sections on management unless otherwise noted but are included in the discussion of prevention. This guideline will not address long-term sequelae of bronchiolitis, such as recurrent wheezing or risk of asthma, which is a field with a large and distinct literature.

Bronchiolitis is a disorder commonly caused by viral lower respiratory tract infection in infants. Bronchiolitis is characterized by acute inflammation, edema, and necrosis of epithelial cells lining small airways, and increased mucus production. Signs and symptoms typically begin with rhinitis and cough, which may progress to tachypnea, wheezing, rales, use of accessory muscles, and/or nasal flaring.[2]

Many viruses that infect the respiratory system cause a similar constellation of signs and symptoms. The most common etiology of bronchiolitis is respiratory syncytial virus (RSV), with the highest incidence of infection occurring between December and March in North America. Some regional variations occur (Fig 1). Ninety percent of children are infected with RSV by the first 2 years of life,[5] and up to 40% will experience lower respiratory tract

infection during the initial infection.[6,7] Infection with RSV does not grant permanent or long-term immunity, with reinfections common throughout life.[8] Other viruses that cause bronchiolitis include human rhinovirus, human metapneumovirus, influenza, adenovirus, coronavirus, human, and parainfluenza viruses. In a study of inpatients and outpatients with bronchiolitis,[9] 76% of patients had RSV, 39% had human rhinovirus, 10% had influenza, 2% had coronavirus, 3% had human metapneumovirus, and 1% had parainfluenza viruses (some patients had coinfections, so the total is greater than 100%).

FIGURE 1



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RSV season by US regions. Centers for Disease Control and Prevention. RSV activity—United States, July 2011–Jan 2013. *MMWR Morb Mortal Wkly Rep*. 2013;62(8):141–144.

States at an estimated cost of $1.73 billion.[10] One prospective, population-based study sponsored by the Centers for Disease Control and Prevention reported the average RSV hospitalization rate was 5.2 per 1000 children younger than 24 months of age during the 5-year period between 2000 and 2005.[11] The highest age-specific rate of RSV hospitalization occurred among infants between 30 days and 60 days of age (25.9 per 1000 children). For preterm infants (<37 weeks' gestation), the RSV hospitalization rate was 4.6 per 1000 children, a number similar to the RSV hospitalization rate for term infants of 5.2 per 1000. Infants born at <30 weeks' gestation had the highest hospitalization rate at 18.7 children per 1000, although the small number of infants born before 30 weeks' gestation make this number unreliable. Other studies indicate the RSV hospitalization rate in extremely preterm infants is similar to that of term infants.[12,13]

Methods

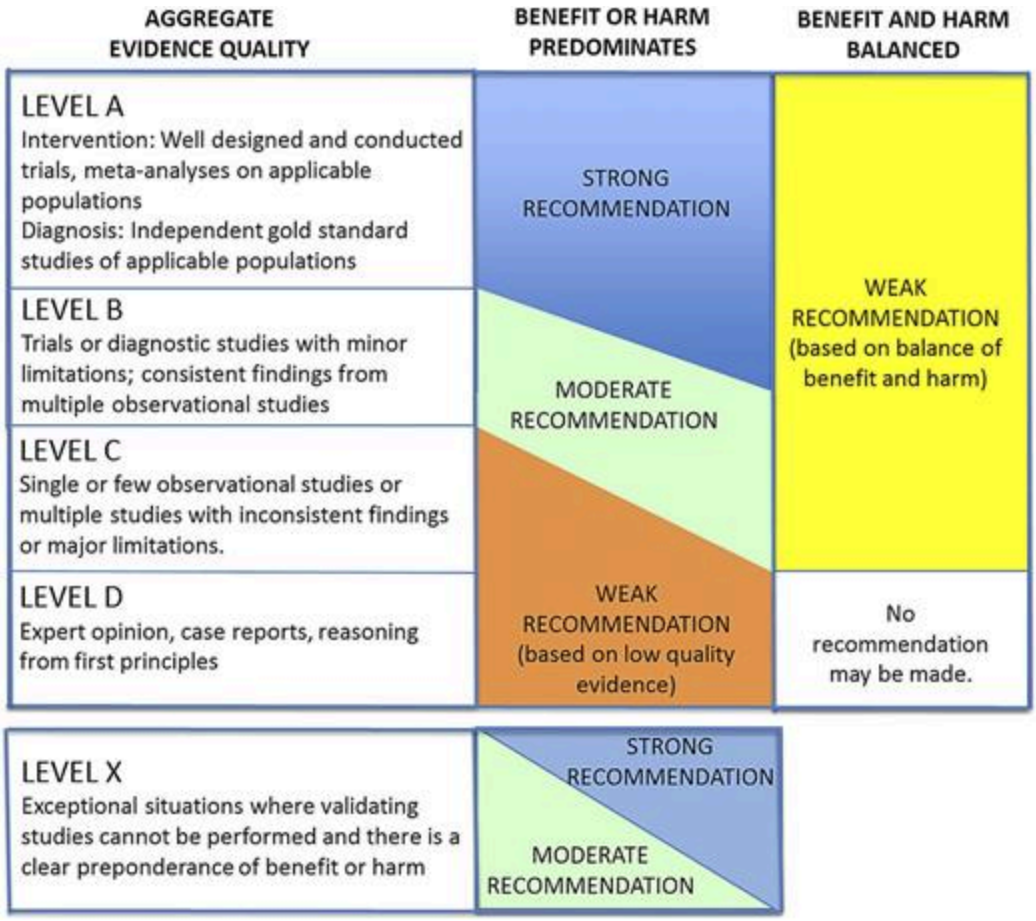
In June 2013, the AAP convened a new subcommittee to review and revise the 2006 bronchiolitis guideline. The subcommittee included primary care physicians, including general pediatricians, a family physician, and pediatric subspecialists, including hospitalists, pulmonologists, emergency physicians, a neonatologist, and pediatric infectious disease physicians. The subcommittee also included an epidemiologist trained in systematic reviews, a guideline methodologist/informatician, and a parent representative. All panel members reviewed the AAP Policy on Conflict of Interest and Voluntary Disclosure and were given an opportunity to declare any potential conflicts. Any conflicts can be found in the author listing at the end of this guideline. All funding was provided by the AAP, with travel assistance from the American Academy of Family Physicians, the American College of Chest Physicians, the American Thoracic Society, and the American College of Emergency Physicians for their liaisons.

The evidence search and review included electronic database searches in *The Cochrane Library*, Medline via Ovid, and CINAHL via EBSCO. The search strategy is shown in the **Appendix**. Related article searches were conducted in PubMed. The bibliographies of articles identified by database searches were also reviewed by 1 of 4 members of the committee, and references identified in this manner were added to the review. Articles [illegible] guideline were reviewed. In addition, the committee reviewed articles published after

completion of the systematic review for these updated guidelines. The current literature review encompasses the period from 2004 through May 2014.

The evidence-based approach to guideline development requires that the evidence in support of a policy be identified, appraised, and summarized and that an explicit link between evidence and recommendations be defined. Evidence-based recommendations reflect the quality of evidence and the balance of benefit and harm that is anticipated when the recommendation is followed. The AAP policy statement "Classifying Recommendations for Clinical Practice"[14] was followed in designating levels of recommendation (Fig 2; Table 1).

FIGURE 2



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Integrating evidence quality appraisal with an assessment of the anticipated balance of benefits and harms leads to designation of a strong recommendation, moderate recommendation, or weak recommendation.

TABLE 1 Guideline Definitions for Evidence-Based Statements

Statement	Definition	Implication
Strong recommendation	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa), and quality of evidence is excellent or unobtainable.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate recommendation	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa), and the quality of evidence is good but not excellent (or is unobtainable).	Clinicians would be prudent to follow a moderate recommendation but should remain alert to new information and sensitive to patient preferences.
Weak recommendation (based on low-quality evidence	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa), but the quality of evidence is weak.	Clinicians would be prudent to follow a weak recommendation but should remain alert to new information and very sensitive to patient preferences.
Weak recommendation (based on balance of benefits and harms)	Weak recommendation is provided when the aggregate database shows evidence of both benefit and harm that appear similar in magnitude for any available courses of action	Clinicians should consider the options in their decision making, but patient preference may have a substantial role.

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A draft version of this clinical practice guideline underwent extensive peer review by committees, councils, and sections within AAP; the American Thoracic Society, American College of Chest Physicians, American Academy of Family Physicians, and American College of Emergency Physicians; other outside organizations; and other individuals identified by the subcommittee as experts in the field. The resulting comments were reviewed by the subcommittee and, when appropriate, incorporated into the guideline.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with bronchiolitis. Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or establish a protocol for the care of all children with bronchiolitis. These recommendations may not provide the only appropriate approach to the management of children with bronchiolitis.

All AAP guidelines are reviewed every 5 years.

Diagnosis

Key Action Statement 1a

Clinicians should diagnose bronchiolitis and assess disease severity on the basis of history and physical examination (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 1a

Aggregate evidence quality	B
Benefits	Inexpensive, noninvasive, accurate
Risk, harm, cost	Missing other diagnoses
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

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Key Action Statement 1b

Clinicians should assess risk factors for severe disease, such as age <12 weeks, a history of prematurity, underlying cardiopulmonary disease, or immunodeficiency.

Action Statement Profile KAS 1b

Aggregate evidence quality	B
Benefits	Improved ability to predict course of illness, appropriate disposition
Risk, harm, cost	Possible unnecessary hospitalization parental anxiety
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	“Assess” is not defined
Role of patient preferences	None
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None

View large

Key Action Statement 1c

When clinicians diagnose bronchiolitis on the basis of history and physical examination, radiographic or laboratory studies should not be obtained routinely (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 1b

Aggregate evidence quality	B
Benefits	Decreased radiation exposure, noninvasive (less procedure-associated discomfort), decreased antibiotic use, cost savings, time saving
Risk, harm, cost	Misdiagnosis, missed diagnosis of comorbid condition
Benefit-harm assessment	Benefits outweigh harms

Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	Infants and children with unexpected worsening disease
Strength	Moderate recommendation
Differences of opinion	None

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The main goals in the history and physical examination of infants presenting with wheeze or other lower respiratory tract symptoms, particularly in the winter season, is to differentiate infants with probable viral bronchiolitis from those with other disorders. In addition, an estimate of disease severity (increased respiratory rate, retractions, decreased oxygen saturation) should be made. Most clinicians recognize bronchiolitis as a constellation of clinical signs and symptoms occurring in children younger than 2 years, including a viral upper respiratory tract prodrome followed by increased respiratory effort and wheezing. Clinical signs and symptoms of bronchiolitis consist of rhinorrhea, cough, tachypnea, wheezing, rales, and increased respiratory effort manifested as grunting, nasal flaring, and intercostal and/or subcostal retractions.

The course of bronchiolitis is variable and dynamic, ranging from transient events, such as apnea, to progressive respiratory distress from lower airway obstruction. Important issues to assess in the history include the effects of respiratory symptoms on mental status, feeding, and hydration. The clinician should assess the ability of the family to care for the child and to return for further evaluation if needed. History of underlying conditions, such as prematurity, cardiac disease, chronic pulmonary disease, immunodeficiency, or episodes of previous wheezing, should be identified. Underlying conditions that may be associated with an increased risk of progression to severe disease or mortality include hemodynamically significant congenital heart disease, chronic lung disease (bronchopulmonary dysplasia),

congenital anomalies,[15,17] in utero smoke exposure,[18] and the presence of an immunocompromising state.[19,20] In addition, genetic abnormalities have been associated with more severe presentation with bronchiolitis.[21]

Assessment of a child with bronchiolitis, including the physical examination, can be complicated by variability in the disease state and may require serial observations over time to fully assess the child's status. Upper airway obstruction contributes to work of breathing. Suctioning and positioning may decrease the work of breathing and improve the quality of the examination. Respiratory rate in otherwise healthy children changes considerably over the first year of life.[22,25] In hospitalized children, the 50th percentile for respiratory rate decreased from 41 at 0 to 3 months of age to 31 at 12 to 18 months of age.[26] Counting respiratory rate over the course of 1 minute is more accurate than shorter observations.[27] The presence of a normal respiratory rate suggests that risk of significant viral or bacterial lower respiratory tract infection or pneumonia in an infant is low (negative likelihood ratio approximately 0.5),[27,29] but the presence of tachypnea does not distinguish between viral and bacterial disease.[30,31]

The evidence relating the presence of specific findings in the assessment of bronchiolitis to clinical outcomes is limited. Most studies addressing this issue have enrolled children when presenting to hospital settings, including a large, prospective, multicenter study that assessed a variety of outcomes from the emergency department (ED) and varied inpatient settings.[18,32,33] Severe adverse events, such as ICU admission and need for mechanical ventilation, are uncommon among children with bronchiolitis and limit the power of these studies to detect clinically important risk factors associated with disease progression.[16,34,35] Tachypnea, defined as a respiratory rate ≥70 per minute, has been associated with increased risk of severe disease in some studies[35,37] but not others.[38] Many scoring systems have been developed in an attempt to objectively quantify respiratory distress, although none has achieved widespread acceptance and few have demonstrated any predictive validity, likely because of the substantial temporal variability in physical findings in infants with bronchiolitis.[39]

Pulse oximetry has been rapidly adopted into clinical assessment of children with bronchiolitis on the basis of data suggesting that it reliably detects hypoxemia not suspected on physical examination[36,40]; however, few studies have assessed the effectiveness of pulse oximetry to predict clinical outcomes. Among inpatients, perceived

need for supplemental oxygen on the basis of pulse oximetry has been associated with prolonged hospitalization, ICU admission, and mechanical ventilation.[16,34,41] Among outpatients, available evidence differs on whether mild reductions in pulse oximetry (<95% on room air) predict progression of disease or need for a return observational visit.[38]

Apnea has been reported to occur with a wide range of prevalence estimates and viral etiologies.[42,43] Retrospective, hospital-based studies have included a high proportion of infants with risk factors, such as prematurity or neuromuscular disease, that may have biased the prevalence estimates. One large study found no apnea events for infants assessed as low risk by using several risk factors: age >1 month for full-term infants or 48 weeks' postconceptional age for preterm infants, and absence of any previous apneic event at presentation to the hospital.[44] Another large multicenter study found no association between the specific viral agent and risk of apnea in bronchiolitis.[42]

The literature on viral testing for bronchiolitis has expanded in recent years with the availability of sensitive polymerase chain reaction (PCR) assays. Large studies of infants hospitalized for bronchiolitis have consistently found that 60% to 75% have positive test results for RSV, and have noted coinfections in up to one-third of infants.[32,33,45] In the event an infant receiving monthly prophylaxis is hospitalized with bronchiolitis, testing should be performed to determine if RSV is the etiologic agent. If a breakthrough RSV infection is determined to be present based on antigen detection or other assay, monthly palivizumab prophylaxis should be discontinued because of the very low likelihood of a second RSV infection in the same year. Apart from this setting, routine virologic testing is not recommended.

Infants with non-RSV bronchiolitis, in particular human rhinovirus, appear to have a shorter courses and may represent a different phenotype associated with repeated wheezing.[32] PCR assay results should be interpreted cautiously, given that the assay may detect prolonged viral shedding from an unrelated previous illness, particularly with rhinovirus. In contrast, RSV detected by PCR assay almost always is associated with disease. At the individual patient level, the value of identifying a specific viral etiology causing bronchiolitis has not been demonstrated.[33]

Atelectasis on chest radiography was associated with increased risk of severe disease in 1 outpatient study.[16] Further studies, including 1 randomized trial, suggest children with suspected lower respiratory tract infection who had radiography performed were more likely to receive antibiotics without any difference in outcomes.[46,47] Initial radiography should be reserved for cases in which respiratory effort is severe enough to warrant ICU admission or where signs of an airway complication (such as pneumothorax) are present.

Treatment

Albuterol

Key Action Statement 2

Clinicians should not administer albuterol (or salbutamol) to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 2

Aggregate evidence quality	B
Benefits	Avoid adverse effects, avoid ongoing use of ineffective medication, lower costs
Risk, harm, cost	Missing transient benefit of drug
Benefit-harm assessment	Benefits outweigh harms
Value judgments	Overall ineffectiveness outweighs possible transient benefit
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
[illegible]	None

Notes	This guideline no longer recommends a trial of albuterol, as was considered in the 2006 AAP bronchiolitis guideline

View large

Although several studies and reviews have evaluated the use of bronchodilator medications for viral bronchiolitis, most randomized controlled trials have failed to demonstrate a consistent benefit from α- or β-adrenergic agents. Several meta-analyses and systematic reviews[48,-53] have shown that bronchodilators may improve clinical symptom scores, but they do not affect disease resolution, need for hospitalization, or length of stay (LOS). Because clinical scores may vary from one observer to the next[39,54] and do not correlate with more objective measures, such as pulmonary function tests,[55] clinical scores are not validated measures of the efficacy of bronchodilators. Although transient improvements in clinical score have been observed, most infants treated with bronchodilators will not benefit from their use.

A recently updated Cochrane systematic review assessing the impact of bronchodilators on oxygen saturation, the primary outcome measure, reported 30 randomized controlled trials involving 1992 infants in 12 countries.[56] Some studies included in this review evaluated agents other than albuterol/salbutamol (eg, ipratropium and metaproterenol) but did not include epinephrine. Small sample sizes, lack of standardized methods for outcome evaluation (eg, timing of assessments), and lack of standardized intervention (various bronchodilators, drug dosages, routes of administration, and nebulization delivery systems) limit the interpretation of these studies. Because of variable study designs as well as the inclusion of infants who had a history of previous wheezing in some studies, there was considerable heterogeneity in the studies. Sensitivity analysis (ie, including only studies at low risk of bias) significantly reduced heterogeneity measures for oximetry while having little effect on the overall effect size of oximetry (mean difference [MD] –0.38, 95% confidence interval [CI] –0.75 to 0.00). Those studies showing benefit[57,-59] are methodologically weaker than other studies and include older children with recurrent wheezing. Results of the Cochrane review indicated no benefit in the clinical course of infants with bronchiolitis who received bronchodilators. The potential adverse effects (tachycardia and tremor) and cost of these agents outweigh any potential benefits.

In the previous iteration of this guideline, a trial of β-agonists was included as an option. However, given the greater strength of the evidence demonstrating no benefit, and that there is no well-established way to determine an "objective method of response" to bronchodilators in bronchiolitis, this option has been removed. Although it is true that a small subset of children with bronchiolitis may have reversible airway obstruction resulting from smooth muscle constriction, attempts to define a subgroup of responders have not been successful to date. If a clinical trial of bronchodilators is undertaken, clinicians should note that the variability of the disease process, the host's airway, and the clinical assessments, particularly scoring, would limit the clinician's ability to observe a clinically relevant response to bronchodilators.

Chavasse et al[60] reviewed the available literature on use of β-agonists for children younger than 2 years with recurrent wheezing. At the time of that review, there were 3 studies in the outpatient setting, 2 in the ED, and 3 in the pulmonary function laboratory setting. This review concluded there were no clear benefits from the use of β-agonists in this population. The authors noted some conflicting evidence, but further study was recommended only if the population could be clearly defined and meaningful outcome measures could be identified.

The population of children with bronchiolitis studied in most trials of bronchodilators limits the ability to make recommendations for all clinical scenarios. Children with severe disease or with respiratory failure were generally excluded from these trials, and this evidence cannot be generalized to these situations. Studies using pulmonary function tests show no effect of albuterol among infants hospitalized with bronchiolitis.[56,61] One study in a critical care setting showed a small decrease in inspiratory resistance after albuterol in one group and levalbuterol in another group, but therapy was accompanied by clinically significant tachycardia.[62] This small clinical change occurring with significant adverse effects does not justify recommending albuterol for routine care.

Epinephrine

Key Action Statement 3

Clinicians should not prescribe nebulized epinephrine in the routine diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 3

Aggregate evidence quality	B
Benefits	Avoiding adverse effects, lower costs, avoiding ongoing use of ineffective medication
Risk, harm, cost	Missing transient benefit of drug
Benefit-harm assessment	Benefits outweigh harms
Value judgments	The overall ineffectiveness outweighs possible transient benefit
Intentional vagueness	None
Role of patient preferences	None
Exclusions	Rescue treatment of rapidly deteriorating patients
Strength	Strong recommendation
Differences of opinion	None

View large

Epinephrine is an adrenergic agent with both β- and α-receptor agonist activity that has been used to treat upper and lower respiratory tract illnesses both as a systemic agent and directly into the respiratory tract, where it is typically administered as a nebulized solution. Nebulized epinephrine has been administered in the racemic form and as the purified L-enantiomer, which is commercially available in the United States for intravenous use. Studies in other diseases, such as croup, have found no difference in efficacy on the basis of preparation,[63] although the comparison has not been specifically studied for bronchiolitis. Most studies have compared L-epinephrine to placebo or albuterol. A recent Cochrane meta-analysis by Hartling et al[64] systematically evaluated the evidence on this topic and found no evidence for utility in the inpatient setting. Two large, multicenter randomized trials comparing nebulized epinephrine to placebo[65] or albuterol[66] in the hospital setting found no improvement in LOS or other inpatient outcomes. A recent, large, multicenter trial found a similar lack of efficacy compared with placebo and further demonstrated longer LOS when epinephrine was used on a fixed schedule compared with an as-needed

schedule.[67] This evidence suggests epinephrine should not be used in children hospitalized for bronchiolitis, except potentially as a rescue agent in severe disease, although formal study is needed before a recommendation for the use of epinephrine in this setting.

The role of epinephrine in the outpatient setting remains controversial. A major addition to the evidence base came from the Canadian Bronchiolitis Epinephrine Steroid Trial.[68] This multicenter randomized trial enrolled 800 patients with bronchiolitis from 8 EDs and compared hospitalization rates over a 7-day period. This study had 4 arms: nebulized epinephrine plus oral dexamethasone, nebulized epinephrine plus oral placebo, nebulized placebo plus oral dexamethasone, and nebulized placebo plus oral placebo. The group of patients who received epinephrine concomitantly with corticosteroids had a lower likelihood of hospitalization by day 7 than the double placebo group, although this effect was no longer statistically significant after adjusting for multiple comparisons.

The systematic review by Hartling et al[64] concluded that epinephrine reduced hospitalizations compared with placebo on the day of the ED visit but not overall. Given that epinephrine has a transient effect and home administration is not routine practice, discharging an infant after observing a response in a monitored setting raises concerns for subsequent progression of illness. Studies have not found a difference in revisit rates, although the numbers of revisits are small and may not be adequately powered for this outcome. In summary, the current state of evidence does not support a routine role for epinephrine for bronchiolitis in outpatients, although further data may help to better define this question.

Hypertonic Saline

Key Action Statement 4a

Nebulized hypertonic saline should not be administered to infants with a diagnosis of bronchiolitis in the emergency department (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 4a

Evidence quality	B

Benefits	Avoiding adverse effects, such as wheezing and excess secretions, cost
Risk, harm, cost	None
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None

View large

Key Action Statement 4b

Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis (Evidence Quality: B; Recommendation Strength: Weak Recommendation [based on randomized controlled trials with inconsistent findings]).

Action Statement Profile KAS 4b

Aggregate evidence quality	B
Benefits	May shorten hospital stay if LOS is >72 h
Risk, harm, cost	Adverse effects such as wheezing and excess secretions; cost
Benefit-harm assessment	Benefits outweigh harms for longer hospital stays
Value judgments	Anticipating an individual child's LOS is difficult. Most US hospitals report an average LOS of <72 h for patients with bronchiolitis. This weak recommendation applies only if the average

Intentional vagueness	This weak recommendation is based on an average LOS and does not address the individual patient.
Role of patient preferences	None
Exclusions	None
Strength	Weak
Differences of opinion	None

View large

Nebulized hypertonic saline is an increasingly studied therapy for acute viral bronchiolitis. Physiologic evidence suggests that hypertonic saline increases mucociliary clearance in both normal and diseased lungs.[69,–71] Because the pathology in bronchiolitis involves airway inflammation and resultant mucus plugging, improved mucociliary clearance should be beneficial, although there is only indirect evidence to support such an assertion. A more specific theoretical mechanism of action has been proposed on the basis of the concept of rehydration of the airway surface liquid, although again, evidence remains indirect.[72]

A 2013 Cochrane review[73] included 11 trials involving 1090 infants with mild to moderate disease in both inpatient and emergency settings. There were 6 studies involving 500 inpatients providing data for the analysis of LOS with an aggregate 1-day decrease reported, a result largely driven by the inclusion of 3 studies with relatively long mean length of stay of 5 to 6 days. The analysis of effect on clinical scores included 7 studies involving 640 patients in both inpatient and outpatient settings and demonstrated incremental positive effect with each day posttreatment from day 1 to day 3 (–0.88 MD on day 1, –1.32 MD on day 2, and –1.51 MD on day 3). Finally, Zhang et al[73] found no effect on hospitalization rates in the pooled analysis of 1 outpatient and 3 ED studies including 380 total patients.

Several randomized trials published after the Cochrane review period further informed the current guideline recommendation. Four trials evaluated admission rates from the ED, 3 using 3% saline and 1 using 7% saline.[74,–76] A single trial[76] demonstrated a difference in admission rates from the ED favoring hypertonic saline, although the other 4 studies were

concordant with the studies included in the Cochrane review. However, contrary to the studies included in the Cochrane review, none of the more recent trials reported improvement in LOS and, when added to the older studies for an updated meta-analysis, they significantly attenuate the summary estimate of the effect on LOS.[76,77] Most of the trials included in the Cochrane review occurred in settings with typical LOS of more than 3 days in their usual care arms. Hence, the significant decrease in LOS noted by Zhang et al[73] may not be generalizable to the United States where the average LOS is 2.4 days.[10] One other ongoing clinical trial performed in the United States, unpublished except in abstract form, further supports the observation that hypertonic saline does not decrease LOS in settings where expected stays are less than 3 days.[78]

The preponderance of the evidence suggests that 3% saline is safe and effective at improving symptoms of mild to moderate bronchiolitis after 24 hours of use and reducing hospital LOS in settings in which the duration of stay typically exceeds 3 days. It has not been shown to be effective at reducing hospitalization in emergency settings or in areas where the length of usage is brief. It has not been studied in intensive care settings, and most trials have included only patients with mild to moderate disease. Most studies have used a 3% saline concentration, and most have combined it with bronchodilators with each dose; however, there is retrospective evidence that the rate of adverse events is similar without bronchodilators,[79] as well as prospective evidence extrapolated from 2 trials without bronchodilators.[79,80] A single study was performed in the ambulatory outpatient setting[81]; however, future studies in the United States should focus on sustained usage on the basis of pattern of effects discerned in the available literature.

Corticosteroids

Key Action Statement 5

Clinicians should not administer systemic corticosteroids to infants with a diagnosis of bronchiolitis in any setting (Evidence Quality: A; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 5

quality	A

Benefits	No clinical benefit, avoiding adverse effects
Risk, harm, cost	None
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

View large

Although there is good evidence of benefit from corticosteroids in other respiratory diseases, such as asthma and croup,[82,84] the evidence on corticosteroid use in bronchiolitis is negative. The most recent Cochrane systematic review shows that corticosteroids do not significantly reduce outpatient admissions when compared with placebo (pooled risk ratio, 0.92; 95% CI, 0.78 to 1.08; and risk ratio, 0.86; 95% CI, 0.7 to 1.06, respectively) and do not reduce LOS for inpatients (MD –0.18 days; 95% CI –0.39 to 0.04).[85] No other comparisons showed relevant differences for either primary or secondary outcomes. This review contained 17 trials with 2596 participants and included 2 large ED-based randomized trials, neither of which showed reductions in hospital admissions with treatment with corticosteroids as compared with placebo.[69,86]

One of these large trials, the Canadian Bronchiolitis Epinephrine Steroid Trial, however, did show a reduction in hospitalizations 7 days after treatment with combined nebulized epinephrine and oral dexamethasone as compared with placebo.[69] Although an unadjusted analysis showed a relative risk for hospitalization of 0.65 (95% CI 0.45 to 0.95; $P = .02$) for combination therapy as compared with placebo, adjustment for multiple comparison testing rendered the result insignificant ($P = .07$). These results have generated considerable controversy. Although there is no standard recognized rationale for why combination

epinephrine and dexamethasone would be synergistic in infants with bronchiolitis, evidence in adults and children older than 6 years with asthma shows that adding inhaled long-acting β agonists to moderate/high doses of inhaled corticosteroids allows reduction of the corticosteroid dose by, on average, 60%.[88] Basic science studies focused on understanding the interaction between β agonists and corticosteroids have shown potential mechanisms for why simultaneous administration of these drugs could be synergistic.[89,-92] However, other bronchiolitis trials of corticosteroids administered by using fixed simultaneous bronchodilator regimens have not consistently shown benefit[93,-97]; hence, a recommendation regarding the benefit of combined dexamethasone and epinephrine therapy is premature.

The systematic review of corticosteroids in children with bronchiolitis cited previously did not find any differences in short-term adverse events as compared with placebo.[86] However, corticosteroid therapy may prolong viral shedding in patients with bronchiolitis.[17]

In summary, a comprehensive systematic review and large multicenter randomized trials provide clear evidence that corticosteroids alone do not provide significant benefit to children with bronchiolitis. Evidence for potential benefit of combined corticosteroid and agents with both α- and β-agonist activity is at best tentative, and additional large trials are needed to clarify whether this therapy is effective.

Further, although there is no evidence of short-term adverse effects from corticosteroid therapy, other than prolonged viral shedding, in infants and children with bronchiolitis, there is inadequate evidence to be certain of safety.

Oxygen

Key Action Statement 6a

Clinicians may choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90% in infants and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength: Weak Recommendation [based on low-level evidence and reasoning from first principles]).

Benefits	Decreased hospitalizations, decreased LOS
Risk, harm, cost	Hypoxemia, physiologic stress, prolonged LOS, increased hospitalizations, increased LOS, cost
Benefit-harm assessment	Benefits outweigh harms
Value judgments	Oxyhemoglobin saturation >89% is adequate to oxygenate tissues; the risk of hypoxemia with oxyhemoglobin saturation >89% is minimal
Intentional vagueness	None
Role of patient preferences	Limited
Exclusions	Children with acidosis or fever
Strength	Weak recommendation (based on low-level evidence/reasoning from first principles)
Differences of opinion	None

View large

Key Action Statement 6b

Clinicians may choose not to use continuous pulse oximetry for infants and children with a diagnosis of bronchiolitis (Evidence Quality: C; Recommendation Strength: Weak Recommendation [based on lower-level evidence]).

Action Statement Profile KAS 6b

Aggregate evidence quality	C
Benefits	Shorter LOS, decreased alarm fatigue, decreased cost
Risk, harm, cost	Delayed detection of hypoxemia, delay in appropriate weaning of oxygen
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None

Intentional vagueness	None
Role of patient preferences	Limited
Exclusions	None
Strength	Weak recommendation (based on lower level of evidence)
Differences of opinion	None

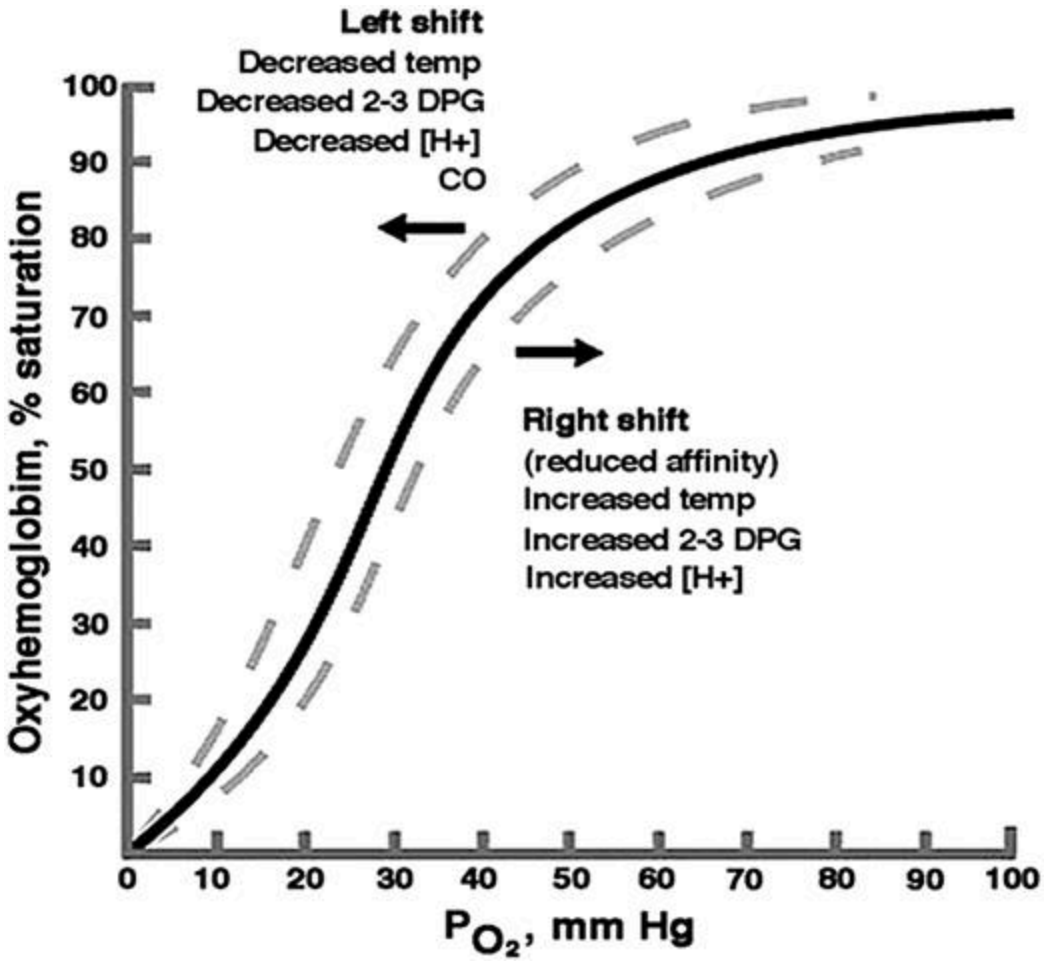
View large

Although oxygen saturation is a poor predictor of respiratory distress, it is associated closely with a perceived need for hospitalization in infants with bronchiolitis.[98,99] Additionally, oxygen saturation has been implicated as a primary determinant of LOS in bronchiolitis.[40,100,101]

Physiologic data based on the oxyhemoglobin dissociation curve (Fig 3) demonstrate that small increases in arterial partial pressure of oxygen are associated with marked improvement in pulse oxygen saturation when the latter is less than 90%; with pulse oxygen saturation readings greater than 90% it takes very large elevations in arterial partial pressure of oxygen to affect further increases. In infants and children with bronchiolitis, no data exist to suggest such increases result in any clinically significant difference in physiologic function, patient symptoms, or clinical outcomes. Although it is well understood that acidosis, temperature, and 2,3-diphosphoglutarate influence the oxyhemoglobin dissociation curve, there has never been research to demonstrate how those influences practically affect infants with hypoxemia. The risk of hypoxemia must be weighed against the risk of hospitalization when making any decisions about site of care. One study of hospitalized children with bronchiolitis, for example, noted a 10% adverse error or near-miss rate for harm-causing interventions.[103] There are no studies on the effect of short-term, brief periods of hypoxemia such as may be seen in bronchiolitis. Transient hypoxemia is common in healthy infants.[104] Travel of healthy children even to moderate altitudes of 1300 m results in transient sleep desaturation to an average of 84% with no known adverse

Although children with chronic hypoxemia do incur developmental and behavioral problems, children who suffer intermittent hypoxemia from diseases such as asthma do not have impaired intellectual abilities or behavioral disturbance.[106–108]

FIGURE 3



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Oxyhemoglobin dissociation curve showing percent saturation of hemoglobin at various partial pressures of oxygen (reproduced with permission from the educational Web site www.anaesthesiauk.com).[102]

Supplemental oxygen provided for infants not requiring additional respiratory support is best initiated with nasal prongs, although exact measurement of fraction of inspired oxygen is unreliable with this method.[109]

Pulse oximetry is a convenient method to assess the percentage of hemoglobin bound by oxygen in children. Pulse oximetry has been erroneously used in bronchiolitis as a proxy for respiratory distress. Accuracy of pulse oximetry is poor, especially in the 76% to 90% range. Further, it has been well demonstrated that oxygen saturation has minimal impact on respiratory drive than carbon dioxide concentrations in the blood.[111] There is very

poor correlation between respiratory distress and oxygen saturations among infants with lower respiratory tract infections.[112] Other than cyanosis, no published clinical sign, model, or score accurately identifies hypoxemic children.[113]

Among children admitted for bronchiolitis, continuous pulse oximetry measurement is not well studied and potentially problematic for children who do not require oxygen. Transient desaturation is a normal phenomenon in healthy infants. In 1 study of 64 healthy infants between 2 weeks and 6 months of age, 60% of these infants exhibited a transient oxygen desaturation below 90%, to values as low as 83%.[105] A retrospective study of the role of continuous measurement of oxygenation in infants hospitalized with bronchiolitis found that 1 in 4 patients incur unnecessarily prolonged hospitalization as a result of a perceived need for oxygen outside of other symptoms[40] and no evidence of benefit was found.

Pulse oximetry is prone to errors of measurement. Families of infants hospitalized with continuous pulse oximeters are exposed to frequent alarms that may negatively affect sleep. Alarm fatigue is recognized by The Joint Commission as a contributor toward in-hospital morbidity and mortality.[114] One adult study demonstrated very poor documentation of hypoxemia alerts by pulse oximetry, an indicator of alarm fatigue.[115] Pulse oximetry probes can fall off easily, leading to inaccurate measurements and alarms.[116] False reliance on pulse oximetry may lead to less careful monitoring of respiratory status. In one study, continuous pulse oximetry was associated with increased risk of minor adverse events in infants admitted to a general ward.[117] The pulse oximetry–monitored patients were found to have less-effective surveillance of their severity of illness when controlling for other variables.

There are a number of new approaches to oxygen delivery in bronchiolitis, 2 of which are home oxygen and high-frequency nasal cannula. There is emerging evidence for the role of home oxygen in reducing LOS or admission rate for infants with bronchiolitis, including 2 randomized trials.[118,119] Most of the studies have been performed in areas of higher altitude, where prolonged hypoxemia is a prime determinant of LOS in the hospital.[120,121] Readmission rates may be moderately higher in patients discharged with home oxygen; however, overall hospital use may be reduced,[122] although not in all settings.[123] Concerns have been raised that home pulse oximetry may complicate care or confuse families.[124] Communication with follow-up physicians is important, because primary care physicians may find difficulty determining safe pulse oximetry levels for discontinuation of oxygen.[125]

Additionally, there may be an increased demand for follow-up outpatient visits associated with home oxygen use.[124]

Use of humidified, heated, high-flow nasal cannula to deliver air-oxygen mixtures provides assistance to infants with bronchiolitis through multiple proposed mechanisms.[126] There is evidence that high-flow nasal cannula improves physiologic measures of respiratory effort and can generate continuous positive airway pressure in bronchiolitis.[127,–130] Clinical evidence suggests it reduces work of breathing[131,132] and may decrease need for intubation,[133,–136] although studies are generally retrospective and small. The therapy has been studied in the ED[136,137] and the general inpatient setting,[134,138] as well as the ICU. The largest and most rigorous retrospective study to date was from Australia,[138] which showed a decline in intubation rate in the subgroup of infants with bronchiolitis (*n* = 330) from 37% to 7% after the introduction of high-flow nasal cannula, while the national registry intubation rate remained at 28%. A single pilot for a randomized trial has been published to date.[139] Although promising, the absence of any completed randomized trial of the efficacy of high-flow nasal cannula in bronchiolitis precludes specific recommendations on it use at present. Pneumothorax is a reported complication.

Chest Physiotherapy

Key Action Statement 7

Clinicians should not use chest physiotherapy for infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 7

Aggregate evidence quality	B
Benefits	Decreased stress from therapy, reduced cost
Risk, harm, cost	None
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None

Role of patient preferences	None
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None

View large

Airway edema, sloughing of respiratory epithelium into airways, and generalized hyperinflation of the lungs, coupled with poorly developed collateral ventilation, put infants with bronchiolitis at risk for atelectasis. Although lobar atelectasis is not characteristic of this disease, chest radiographs may show evidence of subsegmental atelectasis, prompting clinicians to consider ordering chest physiotherapy to promote airway clearance. A Cochrane Review[140] found 9 randomized controlled trials that evaluated chest physiotherapy in hospitalized patients with bronchiolitis. No clinical benefit was found by using vibration or percussion (5 trials)[141,-144] or passive expiratory techniques (4 trials).[145,-148] Since that review, a study[149] of the passive expiratory technique found a small, but significant reduction in duration of oxygen therapy, but no other benefits.

Suctioning of the nasopharynx to remove secretions is a frequent practice in infants with bronchiolitis. Although suctioning the nares may provide temporary relief of nasal congestion or upper airway obstruction, a retrospective study reported that deep suctioning[150] was associated with longer LOS in hospitalized infants 2 to 12 months of age. The same study also noted that lapses of greater than 4 hours in noninvasive, external nasal suctioning were also associated with longer LOS. Currently, there are insufficient data to make a recommendation about suctioning, but it appears that routine use of “deep” suctioning[151,153] may not be beneficial.

Antibacterials

Key Action Statement 8

Clinicians should not administer antibacterial medications to infants and children with a diagnosis of bronchiolitis unless there is a concomitant bacterial infection, or a

strong suspicion of one. (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 8

Aggregate evidence quality	B
Benefits	Fewer adverse effects, less resistance to antibacterial agents, lower cost
Risk, harm, cost	None
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	Strong suspicion is not specifically defined and requires clinician judgment. An evaluation for the source of possible serious bacterial infection should be completed before antibiotic use
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

View large

Infants with bronchiolitis frequently receive antibacterial therapy because of fever,[152] young age,[153] and concern for secondary bacterial infection.[154] Early randomized controlled trials[155,156] showed no benefit from routine antibacterial therapy for children with bronchiolitis. Nonetheless, antibiotic therapy continues to be overused in young infants with bronchiolitis because of concern for an undetected bacterial infection. Studies have shown that [illegible] that may be [illegible]. However, a child with a distinct viral syndrome, such as bronchiolitis, has a lower risk (much less than 1%) of bacterial infection of the cerebrospinal fluid or blood.[157]

Ralston et al[158] conducted a systematic review of serious bacterial infections (SBIs) occurring in hospitalized febrile infants between 30 and 90 days of age with bronchiolitis. Instances of bacteremia or meningitis were extremely rare. Enteritis was not evaluated. Urinary tract infection occurred at a rate of approximately 1%, but asymptomatic bacteriuria may have explained this finding. The authors concluded routine screening for SBI among hospitalized febrile infants with bronchiolitis between 30 and 90 days of age is not justified. Limited data suggest the risk of bacterial infection in hospitalized infants with bronchiolitis younger than 30 days of age is similar to the risk in older infants. An abnormal white blood cell count is not useful for predicting a concurrent SBI in infants and young children hospitalized with RSV lower respiratory tract infection.[159] Several retrospective studies support this conclusion.[160–166] Four prospective studies of SBI in patients with bronchiolitis and/or RSV infections also demonstrated low rates of SBI.[167–171]

Approximately 25% of hospitalized infants with bronchiolitis have radiographic evidence of atelectasis, and it may be difficult to distinguish between atelectasis and bacterial infiltrate or consolidation.[169] Bacterial pneumonia in infants with bronchiolitis without consolidation is unusual.[170] Antibiotic therapy may be justified in some children with bronchiolitis who require intubation and mechanical ventilation for respiratory failure.[172,173]

Although acute otitis media (AOM) in infants with bronchiolitis may be attributable to viruses, clinical features generally do not permit differentiation of viral AOM from those with a bacterial component.[174] Two studies address the frequency of AOM in patients with bronchiolitis. Andrade et al[175] prospectively identified AOM in 62% of 42 patients who presented with bronchiolitis. AOM was present in 50% on entry to the study and developed in an additional 12% within 10 days. A subsequent report[176] followed 150 children hospitalized for bronchiolitis for the development of AOM. Seventy-nine (53%) developed AOM, two-thirds within the first 2 days of hospitalization. AOM did not influence the clinical course or laboratory findings of bronchiolitis. The current AAP guideline on AOM[177] recommends that a diagnosis of AOM should include bulging of the tympanic membrane. This is based on bulging being the best indicator for the presence of bacteria in multiple tympanocentesis studies and on 2 articles comparing antibiotic to placebo therapy that used a bulging tympanic membrane as a necessary part of the diagnosis.[178,179] New studies [illegible] terion of [illegible] panic membrane. Refer to the AOM guideline[180] for recommendations regarding the management of AOM.

Nutrition and Hydration

Key Action Statement 9

Clinicians should administer nasogastric or intravenous fluids for infants with a diagnosis of bronchiolitis who cannot maintain hydration orally (Evidence Quality: X; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 9

Aggregate evidence quality	X
Benefits	Maintaining hydration
Risk, harm, cost	Risk of infection, risk of aspiration with nasogastric tube, discomfort, hyponatremia, intravenous infiltration, overhydration
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	Shared decision as to which mode is used
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

View large

The level of respiratory distress attributable to bronchiolitis guides the indications for fluid replacement. Conversely, food intake in the previous 24 hours may be a predictor of oxygen saturation among infants with bronchiolitis. One study found that food intake of less than 50% of normal for the previous 24 hours is associated with a pulse oximetry value of <90%.[1] Infants with mild respiratory distress may require only observation, particularly if

feeding remains unaffected. When the respiratory rate exceeds 60 to 70 breaths per minute, feeding may be compromised, particularly if nasal secretions are copious. There is limited evidence to suggest coordination of breathing with swallowing may be impaired among infants with bronchiolitis.[181] These infants may develop increased nasal flaring, retractions, and prolonged expiratory wheezing when fed and may be at increased risk of aspiration.[182]

One study estimated that one-third of infants hospitalized for bronchiolitis require fluid replacement.[183] One case series[184] and 2 randomized trials,[185,186] examined the comparative efficacy and safety of the intravenous and nasogastric routes for fluid replacement. A pilot trial in Israel that included 51 infants younger than 6 months demonstrated no significant differences in the duration of oxygen needed or time to full oral feeds between infants receiving intravenous 5% dextrose in normal saline solution or nasogastric breast milk or formula.[187] Infants in the intravenous group had a shorter LOS (100 vs 120 hours) but it was not statistically significant. In a larger open randomized trial including infants between 2 and 12 months of age and conducted in Australia and New Zealand, there were no significant differences in rates of admission to ICUs, need for ventilatory support, and adverse events between 381 infants assigned to nasogastric hydration and 378 infants assigned to intravenous hydration.[188] There was a difference of 4 hours in mean LOS between the intravenous group (82.2 hours) and the nasogastric group (86.2 hours) that was not statistically significant. The nasogastric route had a higher success rate of insertion than the intravenous route. Parental satisfaction scores did not differ between the intravenous and nasogastric groups. These studies suggest that infants who have difficulty feeding safely because of respiratory distress can receive either intravenous or nasogastric fluid replacement; however, more evidence is needed to increase the strength of this recommendation.

The possibility of fluid retention related to production of antidiuretic hormone has been raised in patients with bronchiolitis.[187,189] Therefore, receipt of hypotonic fluid replacement and maintenance fluids may increase the risk of iatrogenic hyponatremia in these infants. A recent meta-analysis demonstrated that among hospitalized children requiring maintenance fluids, the use of hypotonic fluids was associated with significant hyponatremia compared with isotonic fluids in older children.[190] Use of isotonic fluids, in general, appears to be safer.

Key Action Statement 10a

Clinicians should not administer palivizumab to otherwise healthy infants with a gestational age of 29 weeks, 0 days or greater (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 10a

Aggregate evidence quality	B
Benefits	Reduced pain of injections, reduced use of a medication that has shown minimal benefit, reduced adverse effects, reduced visits to health care provider with less exposure to illness
Risk, harm, cost	Minimal increase in risk of RSV hospitalization
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	Parents may choose to not accept palivizumab
Exclusions	Infants with chronic lung disease of prematurity and hemodynamically significant cardiac disease (as described in KAS 10b)
Strength	Recommendation
Differences of opinion	None
Notes	This KAS is harmonized with the AAP policy statement on palivizumab

View large

Key Action Statement 10b

Clinicians should administer palivizumab during the first year of life to infants with hemodynamically significant heart disease or chronic lung disease of prematurity

defined as preterm infants <32 weeks, 0 days' gestation who require >21% oxygen for at least the first 28 days of life (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 10b

Aggregate evidence quality	B
Benefits	Reduced risk of RSV hospitalization
Risk, harm, cost	Injection pain; increased risk of illness from increased visits to clinician office or clinic; cost; side effects from palivizumab
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	Parents may choose to not accept palivizumab
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None
Notes	This KAS is harmonized with the AAP policy statement on palivizumab[191,192]

View large

Key Action Statement 10c

Clinicians should administer a maximum 5 monthly doses (15 mg/kg/dose) of palivizumab during the RSV season to infants who qualify for palivizumab in the first year of life (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 10c

Aggregate evidence quality	B
Benefits	Reduced risk of hospitalization; reduced admission to ICU
Risk, harm, cost	Injection pain; increased risk of illness from increased visits to clinician office or clinic; cost; adverse effects of palivizumab
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	Fewer doses should be used if the bronchiolitis season ends before the completion of 5 doses; if the child is hospitalized with a breakthrough RSV, monthly prophylaxis should be discontinued
Strength	Moderate recommendation
Differences of opinion	None
Notes	This KAS is harmonized with the AAP policy statement on palivizumab[191,192]

View large

Detailed evidence to support the policy statement on palivizumab and this palivizumab section can be found in the technical report on palivizumab.[192]

Palivizumab was licensed by the US Food and Drug Administration in June 1998 largely on the basis of results of 1 clinical trial.[193] The results of a second clinical trial among children with congenital heart disease were reported in December 2003.[194] No other prospective, randomized, placebo-controlled trials have been conducted in any subgroup. Since licensure of palivizumab, [illegible] disease caused by RSV.[195–197] As a result of new data, the Bronchiolitis

Guideline Committee and the Committee on Infectious Diseases have updated recommendations for use of prophylaxis.

Prematurity

Monthly palivizumab prophylaxis should be restricted to infants born before 29 weeks, 0 days' gestation, except for infants who qualify on the basis of congenital heart disease or chronic lung disease of prematurity. Data show that infants born at or after 29 weeks, 0 days' gestation have an RSV hospitalization rate similar to the rate of full-term infants.[11,198] Infants with a gestational age of 28 weeks, 6 days or less who will be younger than 12 months at the start of the RSV season should receive a maximum of 5 monthly doses of palivizumab or until the end of the RSV season, whichever comes first. Depending on the month of birth, fewer than 5 monthly doses will provide protection for most infants for the duration of the season.

Congenital Heart Disease

Despite the large number of subjects enrolled, little benefit from palivizumab prophylaxis was found in the industry-sponsored cardiac study among infants in the cyanotic group (7.9% in control group versus 5.6% in palivizumab group, or 23 fewer hospitalizations per1000 children; $P = .285$).[197] In the acyanotic group (11.8% vs 5.0%), there were 68 fewer RSV hospitalizations per 1000 prophylaxis recipients ($P = .003$).[197,199,200]

Chronic Lung Disease of Prematurity

Palivizumab prophylaxis should be administered to infants and children younger than 12 months who develop chronic lung disease of prematurity, defined as a requirement for 28 days of more than 21% oxygen beginning at birth. If a child meets these criteria and is in the first 24 months of life and continues to require supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy within 6 months of the start of the RSV season, monthly prophylaxis should be administered for the remainder of the season.

Number of Doses

Community outbreaks of RSV disease usually begin in November or December, peak in January or February, and end by late March or, at times, in April.[4] Figure 1 shows the 2011–

2012 bronchiolitis season, which is typical of most years. Because 5 monthly doses will provide more than 24 weeks of protective serum palivizumab concentration, administration of more than 5 monthly doses is not recommended within the continental United States. For infants who qualify for 5 monthly doses, initiation of prophylaxis in November and continuation for a total of 5 doses will provide protection into April.[201] If prophylaxis is initiated in October, the fifth and final dose should be administered in February, and protection will last into March for most children.

Second Year of Life

Because of the low risk of RSV hospitalization in the second year of life, palivizumab prophylaxis is not recommended for children in the second year of life with the following exception. Children who satisfy the definition of chronic lung disease of infancy and continue to require supplemental oxygen, chronic corticosteroid therapy, or diuretic therapy within 6 months of the onset of the second RSV season may be considered for a second season of prophylaxis.

Other Conditions

Insufficient data are available to recommend routine use of prophylaxis in children with Down syndrome, cystic fibrosis, pulmonary abnormality, neuromuscular disease, or immune compromise.

Down Syndrome

Routine use of prophylaxis for children in the first year of life with Down syndrome is not recommended unless the child qualifies because of cardiac disease or prematurity.[202]

Cystic Fibrosis

Routine use of palivizumab prophylaxis in patients with cystic fibrosis is not recommended.[203,204] Available studies indicate the incidence of RSV hospitalization in children with cystic fibrosis is low and unlikely to be different from children without cystic fibrosis. No evidence suggests a benefit from palivizumab prophylaxis in patients with cystic fibrosis. [illegible] centers [illegible] in each group was hospitalized because of RSV infection. Although this study was not powered for efficacy, no clinically meaningful differences in outcome were

reported.[205] A survey of cystic fibrosis center directors published in 2009 noted that palivizumab prophylaxis is not the standard of care for patients with cystic fibrosis.[206] If a neonate is diagnosed with cystic fibrosis by newborn screening, RSV prophylaxis should not be administered if no other indications are present. A patient with cystic fibrosis with clinical evidence of chronic lung disease in the first year of life may be considered for prophylaxis.

Neuromuscular Disease and Pulmonary Abnormality

The risk of RSV hospitalization is not well defined in children with pulmonary abnormalities or neuromuscular disease that impairs ability to clear secretions from the lower airway because of ineffective cough, recurrent gastroesophageal tract reflux, pulmonary malformations, tracheoesophageal fistula, upper airway conditions, or conditions requiring tracheostomy. No data on the relative risk of RSV hospitalization are available for this cohort. Selected infants with disease or congenital anomaly that impairs their ability to clear secretions from the lower airway because of ineffective cough may be considered for prophylaxis during the first year of life.

Immunocompromised Children

Population-based data are not available on the incidence or severity of RSV hospitalization in children who undergo solid organ or hematopoietic stem cell transplantation, receive chemotherapy, or are immunocompromised because of other conditions. Prophylaxis may be considered for hematopoietic stem cell transplant patients who undergo transplantation and are profoundly immunosuppressed during the RSV season.[207]

MISCELLANEOUS ISSUES

Prophylaxis is not recommended for prevention of nosocomial RSV disease in the NICU or hospital setting.[208,209]

No evidence suggests palivizumab is a cost-effective measure to prevent recurrent wheezing in children. Prophylaxis should not be administered to reduce recurrent wheezing in later years.[210,211]

Monthly prophylaxis in Alaska Native children who qualify should be determined by locally generated data regarding season onset and end.

Continuation of monthly prophylaxis for an infant or young child who experiences breakthrough RSV hospitalization is not recommended.

Hand Hygiene

Key Action Statement 11a

All people should disinfect hands before and after direct contact with patients, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 11a

Aggregate evidence quality	B
Benefits	Decreased transmission of disease
Risk, harm, cost	Possible hand irritation
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

View large

Key Action Statement 11b

should wash their hands with soap and water (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Action Statement Profile KAS 11b

Aggregate evidence quality	B
Benefits	Less hand irritation
Risk, harm, cost	If there is visible dirt on the hands, hand washing is necessary; alcohol-based rubs are not effective for *Clostridium difficile,* present a fire hazard, and have a slight increased cost
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Strong recommendation
Differences of opinion	None

View large

Efforts should be made to decrease the spread of RSV and other causative agents of bronchiolitis in medical settings, especially in the hospital. Secretions from infected patients can be found on beds, crib railings, tabletops, and toys.[12] RSV, as well as many other viruses, can survive better on hard surfaces than on porous surfaces or hands. It can remain infectious on counter tops for ≥6 hours, on gowns or paper tissues for 20 to 30 minutes, and

It has been shown that RSV can be carried and spread to others on the hands of caregivers.[213] Studies have shown that health care workers have acquired infection by performing activities such as feeding, diaper change, and playing with the RSV-infected infant. Caregivers who had contact only with surfaces contaminated with the infants' secretions or touched inanimate objects in patients' rooms also acquired RSV. In these studies, health care workers contaminated their hands (or gloves) with RSV and inoculated their oral or conjunctival mucosa.[214] Frequent hand washing by health care workers has been shown to reduce the spread of RSV in the health care setting.[215]

The Centers for Disease Control and Prevention published an extensive review of the hand-hygiene literature and made recommendations as to indications for hand washing and hand antisepsis.[216] Among the recommendations are that hands should be disinfected before and after direct contact with every patient, after contact with inanimate objects in the direct vicinity of the patient, and before putting on and after removing gloves. If hands are not visibly soiled, an alcohol-based rub is preferred. In guidelines published in 2009, the World Health Organization also recommended alcohol-based hand-rubs as the standard for hand hygiene in health care.[217] Specifically, systematic reviews show them to remove organisms more effectively, require less time, and irritate skin less often than hand washing with soap or other antiseptic agents and water. The availability of bedside alcohol-based solutions increased compliance with hand hygiene among health care workers.[214]

When caring for hospitalized children with clinically diagnosed bronchiolitis, strict adherence to hand decontamination and use of personal protective equipment (ie, gloves and gowns) can reduce the risk of cross-infection in the health care setting.[215] Other methods of infection control in viral bronchiolitis include education of personnel and family members, surveillance for the onset of RSV season, and wearing masks when anticipating exposure to aerosolized secretions while performing patient care activities. Programs that implement the aforementioned principles, in conjunction with effective hand decontamination and cohorting of patients, have been shown to reduce the spread of RSV in the health care setting by 39% to 50%.[218,219]

Tobacco Smoke

Clinicians should inquire about the exposure of the infant or child to tobacco smoke when assessing infants and children for bronchiolitis (Evidence Quality: C; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 12a

Aggregate evidence quality	C
Benefits	Can identify infants and children at risk whose family may benefit from counseling, predicting risk of severe disease
Risk, harm, cost	Time to inquire
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	Parent may choose to deny tobacco use even though they are, in fact, users
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None

View large

Key Action Statement 12b

Clinicians should counsel caregivers about exposing the infant or child to environmental tobacco smoke and smoking cessation when assessing a child for bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

Aggregate evidence quality	B
Benefits	Reinforces the detrimental effects of smoking, potential to decrease smoking
Risk, harm, cost	Time to counsel
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	None
Role of patient preferences	Parents may choose to ignore counseling
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None
Notes	Counseling for tobacco smoke prevention should begin in the prenatal period and continue in family-centered care and at all well-infant visits

View large

Tobacco smoke exposure increases the risk and severity of bronchiolitis. Strachan and Cook[220] first delineated the effects of environmental tobacco smoke on rates of lower respiratory tract disease in infants in a meta-analysis including 40 studies. In a more recent systematic review, Jones et al[221] found a pooled odds ratio of 2.51 (95% CI 1.96 to 3.21) for tobacco smoke exposure and bronchiolitis hospitalization among the 7 studies specific to the condition. Other investigators have consistently reported tobacco smoke exposure increases both severity of illness and risk of hospitalization for bronchiolitis.[222,-225] The AAP issued a technical report on the risks of secondhand smoke in 2009. The report makes

Despite our knowledge of this important risk factor, there is evidence to suggest health care providers identify fewer than half of children exposed to tobacco smoke in the outpatient, inpatient, or ED settings.[227,-229] Furthermore, there is evidence that counseling parents in these settings is well received and has a measurable impact. Rosen et al[230] performed a meta-analysis of the effects of interventions in pediatric settings on parental cessation and found a pooled risk ratio of 1.3 for cessation among the 18 studies reviewed.

In contrast to many of the other recommendations, protecting children from tobacco exposure is a recommendation that is primarily implemented outside of the clinical setting. As such, it is critical that parents are fully educated about the importance of not allowing smoking in the home and that smoke lingers on clothes and in the environment for prolonged periods.[231] It should be provided in plain language and in a respectful, culturally effective manner that is family centered, engages parents as partners in their child's health, and factors in their literacy, health literacy, and primary language needs.

Breastfeeding

Key Action Statement 13

Clinicians should encourage exclusive breastfeeding for at least 6 months to decrease the morbidity of respiratory infections (Evidence Quality: Grade B; Recommendation Strength: Moderate Recommendation).

Action Statement Profile KAS 13

Aggregate evidence quality	B
Benefits	May reduce the risk of bronchiolitis and other illnesses; multiple benefits of breastfeeding unrelated to bronchiolitis
Risk, harm, cost	None
Benefit-harm assessment	Benefits outweigh risks
Skip to Main Content	None
[illegible]	None

Role of patient preferences	Parents may choose to feed formula rather than breastfeed
Exclusions	None
Strength	Moderate recommendation
Notes	Education on breastfeeding should begin in the prenatal period

View large

In 2012, the AAP presented a general policy on breastfeeding.[232] The policy statement was based on the proven benefits of breastfeeding for at least 6 months. Respiratory infections were shown to be significantly less common in breastfed children. A primary resource was a meta-analysis from the Agency for Healthcare Research and Quality that showed an overall 72% reduction in the risk of hospitalization secondary to respiratory diseases in infants who were exclusively breastfed for 4 or more months compared with those who were formula fed.[233]

The clinical evidence also supports decreased incidence and severity of illness in breastfed infants with bronchiolitis. Dornelles et al[234] concluded that the duration of exclusive breastfeeding was inversely related to the length of oxygen use and the length of hospital stay in previously healthy infants with acute bronchiolitis. In a large prospective study in Australia, Oddy et al[235] showed that breastfeeding for less than 6 months was associated with an increased risk for 2 or more medical visits and hospital admission for wheezing lower respiratory illness. In Japan, Nishimura et al[236] looked at 3 groups of RSV-positive infants defined as full, partial, or token breastfeeding. There were no significant differences in the hospitalization rate among the 3 groups; however, there were significant differences in the duration of hospitalization and the rate of requiring oxygen therapy, both favoring breastfeeding.

Family Education

Key Action Statement 14

Clinicians and nurses should educate personnel and family members on evidence-based diagnosis, treatment, and prevention in bronchiolitis (Evidence Quality: C;

observational studies; Recommendation Strength; Moderate Recommendation).

Action Statement Profile KAS 14

Aggregate evidence quality	C
Benefits	Decreased transmission of disease, benefits of breastfeeding, promotion of judicious use of antibiotics, risks of infant lung damage attributable to tobacco smoke
Risk, harm, cost	Time to educate properly
Benefit-harm assessment	Benefits outweigh harms
Value judgments	None
Intentional vagueness	Personnel is not specifically defined but should include all people who enter a patient's room
Role of patient preferences	None
Exclusions	None
Strength	Moderate recommendation
Differences of opinion	None

View large

Shared decision-making with parents about diagnosis and treatment of bronchiolitis is a key tenet of patient-centered care. Despite the absence of effective therapies for viral bronchiolitis, caregiver education by clinicians may have a significant impact on care patterns in the disease. Children with bronchiolitis typically suffer from symptoms for 2 to 3 weeks, and parents often seek care in multiple settings during that time period.[237] Given that children with RSV generally shed virus for 1 to 2 weeks and from 30% to 70% of family

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visitors to newborns during the respiratory virus season should be considered. Consistent evidence suggests that parental education is helpful in the

promotion of judicious use of antibiotics and that clinicians may misinterpret parental expectations about therapy unless the subject is openly discussed.[240,–242]

Future Research Needs

- Better algorithms for predicting the course of illness
- Impact of clinical score on patient outcomes
- Evaluating different ethnic groups and varying response to treatments
- Does epinephrine alone reduce admission in outpatient settings?
- Additional studies on epinephrine in combination with dexamethasone or other corticosteroids
- Hypertonic saline studies in the outpatient setting and in in hospitals with shorter LOS
- More studies on nasogastric hydration
- More studies on tonicity of intravenous fluids
- Incidence of true AOM in bronchiolitis by using 2013 guideline definition
- More studies on deep suctioning and nasopharyngeal suctioning
- Strategies for monitoring oxygen saturation
- Use of home oxygen
- Appropriate cutoff for use of oxygen in high altitude
- Oxygen delivered by high-flow nasal cannula
- RSV vaccine and antiviral agents
- Use of palivizumab in special populations, such as cystic fibrosis, neuromuscular diseases, Down syndrome, immune deficiency
- Emphasis on parent satisfaction/patient-centered outcomes in all research (ie, not LOS as the only measure)

Subcommittee on Bronchiolitis (Oversight by the Council on Quality Improvement and Patient Safety, 2013–2014)

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APPENDIX 1 Search Terms by Topic

Introduction

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

1. and exp Natural History/
2. and exp Epidemiology/
3. and (exp economics/ or exp “costs and cost analysis”/ or exp “cost allocation”/ or exp cost-benefit analysis/ or exp “cost control”/ or exp “cost of illness”/ or exp “cost sharing”/
4. and exp Risk Factors/

Limit to English Language AND Humans AND (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”) AND (“natural history” OR (MM “Epidemiology”) OR (MM “Costs and Cost Analysis”) OR (MM “Risk Factors”))

The Cochrane Library

Bronchiolitis AND (epidemiology OR risk factor OR cost)

Diagnosis/Severity

MedLine

exp BRONCHIOLITIS/di [Diagnosis] OR exp Bronchiolitis, Viral/di [Diagnosis]

limit to English Language AND (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

(MH “Bronchiolitis/DI”)

The Cochrane Library

Bronchiolitis AND Diagnosis

*Upper Respiratory Infection Symptoms

MedLine

(exp Bronchiolitis/ OR exp Bronchiolitis, Viral/) AND exp *Respiratory Tract Infections/

Limit to English Language

Limit to “all infant (birth to 23 months)” OR “newborn infant (birth to 1 month)” OR “infant (1 to 23 months)”)

(MM “Bronchiolitis+”) AND (MM “Respiratory Tract Infections+”)

The Cochrane Library

Bronchiolitis AND Respiratory Infection

Inhalation Therapies

*Bronchodilators & Corticosteroids

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

AND (exp Receptors, Adrenergic, β-2/ OR exp Receptors, Adrenergic, β/ OR exp Receptors, Adrenergic, β-1/ OR β adrenergic*.mp. OR exp ALBUTEROL/ OR levalbuterol.mp. OR exp EPINEPHRINE/ OR exp Cholinergic Antagonists/ OR exp IPRATROPIUM/ OR exp Anti-Inflammatory Agents/ OR ics.mp. OR inhaled corticosteroid*.mp. OR exp Adrenal Cortex Hormones/ OR exp Leukotriene Antagonists/ OR montelukast.mp. OR exp Bronchodilator Agents/)

Limit to English Language AND (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”) AND (MM “Bronchodilator Agents”)

The Cochrane Library

Bronchiolitis AND (bronchodilator OR epinephrine OR albuterol OR salbutamol OR corticosteroid OR steroid)

*Hypertonic Saline

MedLine

AND (exp Saline Solution, Hypertonic/ OR (aerosolized saline.mp. OR (exp AEROSOLS/ AND exp Sodium Chloride/)) OR (exp Sodium Chloride/ AND exp “Nebulizers and Vaporizers”/) OR nebulized saline.mp.)

Limit to English Language

Limit to “all infant (birth to 23 months)” OR “newborn infant (birth to 1 month)” OR “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”) AND (MM “Saline Solution, Hypertonic”)

The Cochrane Library

Bronchiolitis AND Hypertonic Saline

Oxygen

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

1. AND (exp Oxygen Inhalation Therapy/ OR supplemental oxygen.mp. OR oxygen saturation.mp. OR *Oxygen/ad,st [Administration & Dosage, Standards] OR oxygen treatment.mp.)
2. AND (exp OXIMETRY/ OR oximeters.mp.) AND (exp “Reproducibility of Results”/ OR reliability.mp. OR function.mp. OR technical specifications.mp.) OR (percutaneous measurement*.mp. OR exp Blood Gas Analysis/)

Limit to English Language

Limit to “all infant (birth to 23 months)” OR “newborn infant (birth to 1 month)” OR “infant (1 to 23 months)”)

((MM “Oxygen Therapy”) OR (MM “Oxygen+”) OR (MM “Oxygen Saturation”) OR (MM “Oximetry+”) OR (MM “Pulse Oximetry”) OR (MM “Blood Gas Monitoring, Transcutaneous”))

The Cochrane Library

Bronchiolitis AND (oxygen OR oximetry)

Chest Physiotherapy and Suctioning

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

1. AND (Chest physiotherapy.mp. OR (exp Physical Therapy Techniques/ AND exp Thorax/))
2. AND (Nasal Suction.mp. OR (exp Suction/))

Limit to English Language

Limit to “all infant (birth to 23 months)” OR “newborn infant (birth to 1 month)” OR “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”)

1. AND ((MH “Chest Physiotherapy (Saba CCC)”) OR (MH “Chest Physical Therapy+”) OR (MH “Chest Physiotherapy (Iowa NIC)”))
2. AND (MH “Suctioning, Nasopharyngeal”)

The Cochrane Library

Bronchiolitis AND (chest physiotherapy OR suction*)

Hydration

AND (exp Fluid Therapy/ AND (exp infusions, intravenous OR exp administration, oral))

Limit to English Language

Limit to (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”) AND

((MM “Fluid Therapy+”) OR (MM “Hydration Control (Saba CCC)”) OR (MM “Hydration (Iowa NOC)”))

The Cochrane Library

Bronchiolitis AND (hydrat* OR fluid*)

SBI and Antibacterials

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

AND

(exp Bacterial Infections/ OR exp Bacterial Pneumonia/ OR exp Otitis Media/ OR exp Meningitis/ OR exp *Anti-bacterial Agents/ OR exp Sepsis/ OR exp Urinary Tract Infections/ OR exp Bacteremia/ OR exp Tracheitis OR serious bacterial infection.mp.)

Limit to English Language

Limit to (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

((MM “Pneumonia, Bacterial+”) OR (MM “Bacterial Infections+”) OR (MM “Otitis Media+”) OR (MM “Meningitis, Bacterial+”) OR (MM “Antiinfective Agents+”) OR (MM “Sepsis+”) OR (MM “Urinary Tract Infections+”) OR (MM “Bacteremia”))

The Cochrane Library

Bronchiolitis AND (serious bacterial infection OR sepsis OR otitis media OR meningitis OR urinary tract infection or bacteremia OR pneumonia OR antibacterial OR antimicrobial OR antibiotic)

Hand Hygiene, Tobacco, Breastfeeding, Parent Education

MedLine

((“bronchiolitis”[MeSH]) OR (“respiratory syncytial viruses”[MeSH]) NOT “bronchiolitis obliterans”[All Fields])

1. AND (exp Hand Disinfection/ OR hand decontamination.mp. OR handwashing.mp.)
2. AND exp Tobacco/
3. AND (exp Breast Feeding/ OR exp Milk, Human/ OR exp Bottle Feeding/)

Limit to English Language

Limit to (“all infant (birth to 23 months)” or “newborn infant (birth to 1 month)” or “infant (1 to 23 months)”)

CINAHL

(MM “Bronchiolitis+”)

1. AND (MH “Handwashing+”)
2. AND (MH “Tobacco+”)
3. AND (MH “Breast Feeding+” OR MH “Milk, Human+” OR MH “Bottle Feeding+”)

1. AND (Breast Feeding OR breastfeeding)

2. AND tobacco

3. AND (hand hygiene OR handwashing OR hand decontamination)

AAP	American Academy of Pediatrics
AOM	acute otitis media
CI	confidence interval
ED	emergency department
KAS	Key Action Statement
LOS	length of stay
MD	mean difference
PCR	polymerase chain reaction
RSV	respiratory syncytial virus
SBI	serious bacterial infection

The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

Clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that

time.

Dedicated to the memory of Dr Caroline Breese Hall.

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Subjects: Infectious Diseases

Topics: bronchiolitis, cochrane collaboration, medline

Comments

7 Comments

Oxygen and oxygenation in bronchiolitis

January 15 2015 | Sergio G. Golombek

To the editor Oxygen and oxygenation in bronchiolitis We read in detail the 2014 guidelines on bronchiolitis (1). We agree that pulse oximetry (SpO2) "has been erroneously used in bronchiolitis as a proxy for respiratory distress". However, the recommendations made about SpO2 may lead to inadequate changes in clinical practice with negative impact for children all over the world. The physiology of oxygenation and the relation of hemoglobin and O2 are fascinating. If as recommended "clinicians choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90%" the risk would be tissue hypoxia. SpO2 of 90% may be associated with low PaO2, O2 content and O2 delivery, more so with

low hemoglobin concentration. Of course, other variables involved in the complex process of oxygenation should not be ignored either (i.e.: cardiac output, temperature, pH, PaCO2 and several others).

The references used that associated prolonged hospitalization, ICU admission, mechanical ventilation and perceived need for supplemental O2 on the basis of pulse oximetry, are from over 20 years ago, when technology was different and understanding of saturation was less than currently. We strongly disagree with "clinicians may choose not to use continuous pulse oximetry". Cyanosis has a poor predictive value of (2) and SpO2 has been considered the fifth vital sign, providing also continuous monitoring of heart rate at no added cost. Not to monitor SpO2 would be similar to choosing not to evaluate, respiratory rate, temperature or other vital signs. Instead of "discarding" SpO2monitoring, it would be more sensible to increase education with the goal to avoid hypoxemia while at the same time avoid inducing hyperoxemia and unnecessary therapy (2).

In 6 A and 6 B, delayed detection of hypoxemia and delay in appropriate weaning of oxygen are both very serious health hazards (2,3). They should not be compared with the potential benefits mentioned (shorter length of stay, decreased alarm fatigue and decreased cost). To improve care and outcomes avoiding health hazards is challenging and must not be oversimplified. The damaging effects of hypoxia are well known, and it is unlikely that any clinician would allow a patient to suffer hypoxia. Giving unnecessary O2could be associated with longer stay and also with hyperoxic induced damage. When infants breathing supplemental O2 have an SpO2 > 95-96%, the PaO2 is high in >60% of the cases (4). FiO2 should be weaned, to avoid associated oxidative stress and oxidative damage.

When "monitored patients are found to have less-effective surveillance of their severity of illnes", the problem is not pulse oximetry but an attitudinal behavior that can improve by improving education.

In summary, current SpO2 monitors vary in specifications, specificity, sensitivity and false alarms. A state of the art monitor and education for its use are essential to significantly decrease or avoid the risks or harm described. To end, we wholeheartedly agree with Dr Modesto i Alapont when he recently wrote that doctors have a moral duty to not repeat mistakes which have harmed patients in the past. (5)

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Conflict of Interest:

None declared

Submitted on January 15 2015

Scientists should learn from their mistakes. And doctors have a moral duty to not repeat mistakes which have harmed patients in the past. A medical paper in 1974 raised concerns about the theory of restricting the use of therapeutic oxygen in infants during neonatal age in order to avoid retinopathy of prematurity. This restriction actually increased perinatal mortality (20,000 babies in England and Wales, 150,000 in USA) (1). The best available evidence indicates that for every 35 (95%CI = 19 to 155) very low birth weight preterm infants in which transcutaneous oxygen saturation (SpO2) levels are maintained to less than 90%, one will die for not receiving enough oxygen during the hospital stay (2). There is no evidence to guide clinical practise regarding the optimal methods for measuring oxygenation, partial pressure of oxygen (PaO2) or SpO2. Currently, monitoring SpO2 levels has largely replaced the practice of monitoring PaO2 and has lowered the range of PaO2 in preterm infants, as compared with previously recommended PaO2 targets. Infants in the lower- target group (SpO2 of 85 to 89%) may have experienced PaO2 levels below 40 mmHg. This severe hypoxemia might have been the cause of those unnecessary deaths (3) and of abnormalities in neurological development at the first months of life.

We have read with interest the 2014 revision of 2006 clinical practice guidelines on bronchiolitis. However, we do not agree with the Key Action Statement 6a. In their reasoning, Ralston SL et al. did not take into account that, if one accepts 90% as the saturation target, the existence of fetal hemoglobin in those infants' blood makes it highly probable that PaO2 levels will be steadily maintained below 40 mmHg. Are not we committing the same mistake again?

The text says, "There are no studies on the effect of short-term, brief periods of hypoxemia such as may be seen in bronchiolitis". The authors justify this with literature regarding asthma, a less hypoxemic illness. But, we believe, this statement is incorrect. Joel L Bass et al. provided evidence showing that chronic or intermittent episodes of hypoxia have adverse impacts on development, behaviour, and academic achievement in children as well as in adults (4). These negative effects have been noted at even mild levels of oxygen desaturation. This should be taken into account in

than 89% is minimal", applied to a population that still has high levels of fetal hemoglobin.

As medical scientists we cannot repeat our great past mistakes. We suggest to target SpO2 in these infants at around 95%, the fifth percentile of the normal basal saturation during the first 6 months of life (5).

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Conflict of Interest:

None declared

Submitted on November 25 2014

Recommendations from committee on treatment of

As a private pediatrician "out in the trenches," I read these recommendations with interest (and a bit of skepticism). First, I am glad that the committee continues to recommend not using CXR's and antibiotics in the initial evaluation of these children. I cannot begin to count the number of children who, in my opinion, have been incorrectly placed on antibiotics for "pneumonia" based upon an chest Xray of a wheezing child. Besides the excess use of antibiotic exposure, the psychological trauma that continues to affect parents when they hear that their child has pneumonia should also be realized. Second, I wonder why or how the committee thinks we should even try to treat bronchiolitis nowadays. I am not to use nebulizer treatments,corticosteroids, nor oxygen. Besides the irrefutable lack of good controlled medical studies available, let alone attempted, using adequate controls (I am a biochemist and 1000, 10,000, or more subjects is grossly inadequate when trying to control individuals with 100's of separate biochemical systems running inside of each of them). These recommendations remind me of the repeated recc's for croup back in the 80's when steroids were specifically discouraged because there was no evidence to support their use. I remember one article published at the time that suggested that these studies failed to show any benefit because the dose of steroids studied had been inadequate. Subsequently, as we all know, corticosteroids are now one of the basics in treatment of common croup. Of course, the problem then is the same now: it is virtually impossible to run all the appropriate control studies required to obtain a truly believable result due to the complexity of the human body and biochemistry, let alone adding in responses to various doses administered at various times, etc. Thank you.

Conflict of Interest:

None declared

Submitted on November 19 2014

Re:The recommendation to not use bronchodilators is not supported by the evidence.

November 3 2014 | Shawn L. Ralston

the concerns raised by Walsh, et al that the guideline ignores the potential clinical benefit of bronchodilators in bronchiolitis, the committee

respectfully disagrees and reiterates our logic. In order to recommend the use of a medication in any disease, the preponderance of benefit should outweigh the likelihood of harm across the entire population for whom the medication is prescribed. While we clearly acknowledged in the guideline that a small proportion of children may appear to get a clinical benefit from bronchodilators (and there is significant disagreement as to whether the magnitude of said benefit is clinically meaningful), the majority of children with bronchiolitis do not stand to benefit. The pathology of early viral wheezing is hypothesized to result from the concomitant effects of viral induced edema and debris in airways that are already small in diameter. A minority of patients with early viral wheezing will also exhibit airway obstruction due to smooth muscle contraction which may be at least partially reversible with bronchodilators. Unfortunately there is no way to reliably distinguish which patients who suffer early wheezing will have reversible airway obstruction. Therefore a recommendation to use albuterol in all patients with first time viral wheezing would mean that the majority of patients given the medication would have no chance of benefiting from it. Such a recommendation would still be acceptable if the consequences of failing to administer the medication to the cohort that is expected to benefit were grave. In the case of bronchiolitis, there is no evidence to suggest such a situation exists, i.e. there is no convincing evidence that albuterol alters meaningful outcomes in bronchiolitis. While a small change in respiratory scores has been interpreted by some to justify the use of the medication in the entire cohort of patients with bronchiolitis, the bronchiolitis committee saw no evidence to suggest that the change in scores was clinically meaningful or that the absence of providing such treatment would substantially harm anyone. Furthermore, the committee felt the harm suffered, including significant side effects and costs, for the majority of patients who would not benefit from the medication outweighed the potential benefit to the much smaller cohort who might respond.

In response to the other concerns raised in the letter, we also disagree with Walsh, et al's interpretation of the existing literature. We would like to point out that evaluation of a therapy against a placebo is considered the highest quality study design and not a weakness; therefore, we fail to see the significance of that particular critique, or of comparing albuterol to epinephrine when placebo controlled trials are available. Finally, we offer no response to Walsh, et al's non-standard use of the term "trend" to

describe clearly negative results in hypothesis testing on the impact of albuterol on hospitalization rates except to note that such usage is expressly forbidden in the instructions to authors for this and most other high quality medical journals.

Shawn Ralston, MD on behalf of the AAP Committee on the Diagnosis and Management of Bronchiolitis

Conflict of Interest:

None declared

Submitted on November 03 2014

The recommendation to not use bronchodilators is not supported by the evidence.

November 2 2014 | Paul Walsh

Dear Editor:

We read with interest the current guidelines on the management of bronchiolitis.(1) Here we raise our concern with the recommendation that bronchodilators not be used.

The guideline authors imply that our RCT of 703 children with bronchiolitis to supports their assertion that "clinical scores may vary from between observers".(1,2) This is a very selective reading of our limitations section. The cited article in fact showed an 18% (aRR 1.18, (95% CI1.02-1.36) relative increase in successful hospital discharges from the emergency department (ED) when albuterol rather than epinephrine was administered. This study also addressed the limitations of consecutive enrollment with random allocation, prior episodes, and study site effect. (2) The severity of illness tool we used has been validated(3) and has adequate interrater agreement (92%;kappa 0.676).

The guideline authors' rely in part on older metanalyses predating this work and on a meta-analysis from 2011 that systematically excluded studies showing a benefit to using albuterol over epinephrine.(4) Therefore these meta-analyses could provide only a limited view of what is known about bronchodilators in bronchiolitis.

The guideline's assertion that bronchodilators should not be used must then rest on the meta-analysis in the Cochrane review library published by Gadomski et al. in 2014.(5) This meta-analysis included only placebo-controlled studies and consequently excluded some studies which showed a benefit between bronchodilators.

However even this 2014 Cochrane review did find a significant benefit to using bronchodilators, OR 0.18 (95%CI 0.06-0.50) as measured by improved clinical scores. (5) In the version cited there were only 187 patients included in the analysis addressing the most important question to emergency physicians and pediatric hospitalists; does albuterol decrease admission from the emergency department. The answer in this meta- analysis showed a non-significant trend towards decreased admission (OR 0.76 (95%CI 0.38-1.53). Even a subsequent analysis with a 404 patients shows (OR 0.77 95%CI 0.44-1.33).(5) This 23% reduction in odds of admission is not dissimilar to the 18% decrease in the relative risk of admission that we found with albuterol.(2)

Neither non-significant underpowered studies nor metanalyses should form the basis for treatment recommendations, any more than null results should form the basis for concluding "no effect".

Given that data from some studies finding a benefit to bronchodilators in the ED has been ignored, and given the actual findings of the 2014 Cochrane review, the recommendation that a bronchodilator not be used is charitably described as weak, particularly for the ED. This recommendation risks doing a disservice to our patients. It is not acceptable for the authors to seek refuge in the statement that this is a guideline and should not be used as the sole guidance for clinical management; experience tells us that is exactly what will happen.

Available evidence clearly suggests that nebulized albuterol decreases hospital admissions from the ED. The guideline should be amended to reflect this.

Yours faithfully

Paul Walsh

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Conflict of Interest:

None declared

Submitted on November 02 2014

Why I will still try albuterol

November 1 2014 | Daniel M Eisenstein

The new clinical practice guidelines for the treatment of bronchiolitis leave no room for the use of albuterol or similar medicines in the treatment of bronchiolitis. The basic reasoning seems sound, in that these medicines have not been shown to change the long term clinical course of affected patients, as measured by such outcomes as length of stay.

I would submit that short term improvements in clinical scores in and of themselves are a compelling reason to treat, since we as physicians are interested in making

though I realize the limitations of individual clinical observations, I would submit it is more than wishful thinking of pediatricians when we believe we see near

term improvements in a subset of our patients with bronchiolitis who are treated with albuterol. Similar to the way ibuprofen does not affect the long term outcome of a broken arm and only treats pain-treating a retracting, air hungry infant with albuterol can considerably improve their comfort.

The danger, of course, is that albuterol only treats the physician's desire to do something, even if that something is totally ineffectual, and perhaps we will be too optimistic when we gauge clinical response and treat more infants with albuterol then we ought to. I would submit that the guidelines should allow physicians to struggle with this issue, rather than pronounce that the use of a safe medication with mild side effects should be effectively forbidden.

Conflict of Interest:

None declared

Submitted on November 01 2014

Pediatric intensive care

November 1 2014 | James A. Lin

Many thanks to the authors for their considerable efforts in updating and publishing this important guideline for management of bronchiolitis. Approximately 5% of infants hospitalized with bronchiolitis require pediatric intensive care.1,2 Would the authors please clarify to what extent pediatric intensivists or the Society of Critical Care Medicine were included in the development of these guidelines? Are the guidelines meant to address clinically severe bronchiolitis?

Sincerely,

James Lin MD Assistant Professor Pediatric Critical Care Medicine David Geffen School of Medicine at UCLA

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children. J Infect Dis.2012;206:178-189.

Conflict of Interest:

None declared

Submitted on November 01 2014

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