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

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CLINICAL PRACTICE GUIDELINE

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

abstract

FREE

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 children 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: *Pediatrics* 2014;134:e1474–e1502

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).
- 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).
- 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]).

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KEY WORDS

bronchiolitis, infants, children, respiratory syncytial virus, evidence-based, guideline

ABBREVIATIONS

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

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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.

All 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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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).
- 29 weeks, 0 days or greater (Evidence Quality: B; Recommendation Strength: Strong Recommendation).
- 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-based diagnosis, treatment, and prevention in bronchiolitis. (Evidence Quality: C; observational studies; Recommendation Strength: Moderate Recommendation).

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,

PREVENTION

- 10a. Clinicians should not administer palivizumab to otherwise healthy infants with a gestational age of

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; however, regional variations occur³ (Fig 1).⁴ Ninety percent of children are infected with RSV in 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 meta-

pneumovirus, 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%).

Bronchiolitis is the most common cause of hospitalization among infants during the first 12 months of life. Approximately 100 000 bronchiolitis admissions occur annually in the United 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

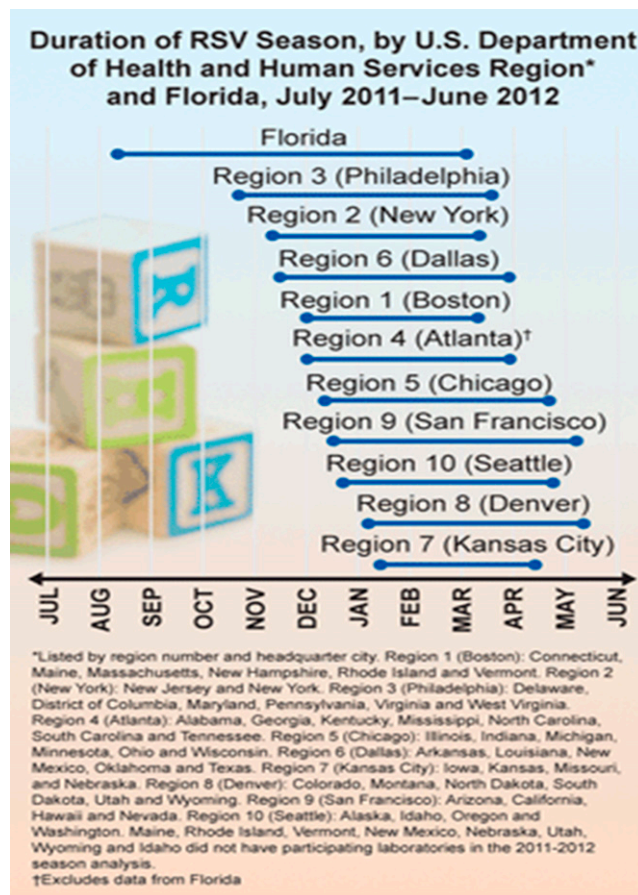


FIGURE 1 RSV season by US regions. Centers for Disease Control and Prevention. RSV activity—United States, July 2011–Jan 2013. *MMWR Morb Mortal Wkly Rep.* 2013;62(8):141–144.

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 included in the 2003 evidence report on bronchiolitis in preparation of the AAP 2006 guideline² also were reviewed. In addition, the committee reviewed articles published after completion of the systematic review for these updated guidelines. The current literature re-

view 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).

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.

AGGREGATE EVIDENCE QUALITY	BENEFIT OR HARM PREDOMINATES	BENEFIT AND HARM BALANCED
LEVEL A Intervention: Well designed and conducted trials, meta-analyses on applicable populations Diagnosis: Independent gold standard studies of applicable populations	STRONG RECOMMENDATION	WEAK RECOMMENDATION (based on balance of benefit and harm)
LEVEL B Trials or diagnostic studies with minor limitations; consistent findings from multiple observational studies	MODERATE RECOMMENDATION	
LEVEL C Single or few observational studies or multiple studies with inconsistent findings or major limitations.	WEAK RECOMMENDATION (based on low quality evidence)	No recommendation may be made.
LEVEL D Expert opinion, case reports, reasoning from first principles		
LEVEL X Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm	STRONG RECOMMENDATION MODERATE RECOMMENDATION	

FIGURE 2

Integrating evidence quality appraisal with an assessment of the anticipated balance between benefits and harms leads to designation of a policy as 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.

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

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, when making decisions about evaluation and management of children with bronchiolitis (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

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	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

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

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

Current evidence does not support routine chest radiography in children with bronchiolitis. Although many infants with bronchiolitis have abnormalities on chest radiography, data are insufficient to demonstrate that chest radiography correlates well with disease severity. 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
Differences of opinion	None
Notes	This guideline no longer recommends a trial of albuterol, as was considered in the 2006 AAP bronchiolitis guideline

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 tremors) 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 al⁶⁰ 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 administer epinephrine to infants and children with a 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

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 al⁶⁴ 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 placebo⁶⁵ or albuterol⁶⁶ 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 al⁶⁴ 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

Aggregate 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

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 length of stay is >72 h
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

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 review⁷³ 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 al⁷³ 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 trial⁷⁶ 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 al⁷³ 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 setting⁸¹; 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

Aggregate evidence 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

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 rendered the result insignificant ($P = .07$). These results have generated considerable controversy.⁸⁷ 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]).

Action Statement Profile KAS 6a

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

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

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 consequences.¹⁰⁵ 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}

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.¹¹⁰ Further, it has been well demonstrated that oxygen saturation has much less 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 symptoms⁴⁰ 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

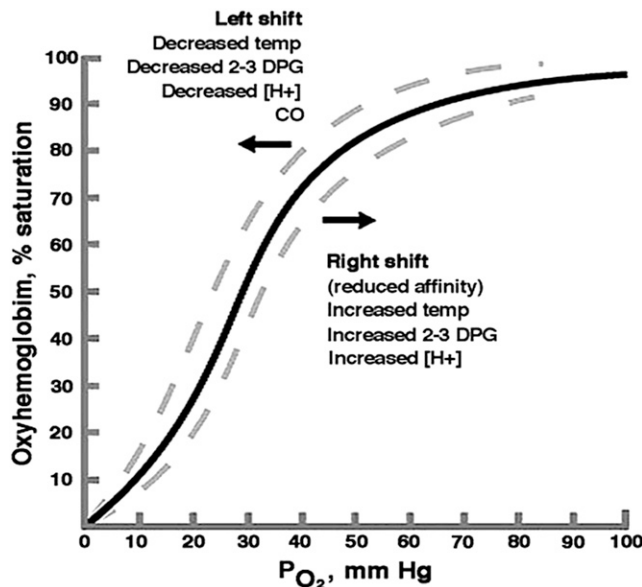


FIGURE 3

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

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, in-

cluding 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 have 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 its 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

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 Review¹⁴⁰ 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 study¹⁴⁹ 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 suctioning¹⁵⁰ 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

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 febrile infants without an identifiable source of fever have a risk of bacteremia that may be as high as 7%. 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 al¹⁵⁸ 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 al¹⁷⁵ 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 report¹⁷⁶ 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 AOM¹⁷⁷ 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 are needed to determine the incidence of AOM in bronchiolitis by using the new criterion of bulging of the tympanic membrane. Refer to the AOM guideline¹⁸⁰ 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

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 bron-

chiolitis. One study found that food intake at less than 50% of normal for the previous 24 hours is associated with a pulse oximetry value of <95%.¹⁸⁰ 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 series¹⁸⁴ 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.

PREVENTION

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

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}

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}

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, new peer-reviewed publications provide greater insight into the epidemiology of 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 per 1000 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 continua-

tion 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. A randomized clinical trial involving 186 children with cystic

fibrosis from 40 centers reported 1 subject 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

Key Action Statement 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).

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 <i>Clostridium difficile</i> , 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

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 on skin for up to 20 minutes.²¹²

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

Key Action Statement 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).

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

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).

Action Statement Profile KAS 12b

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

Tobacco smoke exposure increases the risk and severity of bronchiolitis. Strachan and Cook²²⁰ 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 al²²¹ 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 bronchioli-

tis.^{222–225} The AAP issued a technical report on the risks of secondhand smoke in 2009. The report makes recommendations regarding effective ways to eliminate or reduce secondhand smoke exposure, including education of parents.²²⁶

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 al²³⁰ 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
Value judgments	None
Intentional vagueness	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

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 al²³⁴ 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 al²³⁵ 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 al²³⁶ 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

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 members may become ill,^{238,239} education about prevention of transmission of disease is key. Restriction of 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)

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Shawn L. Ralston, MD, FAAP: Chair, Pediatric Hospitalist (no financial conflicts; published research related to bronchiolitis)

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REFERENCES

1. American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics*. 2006;118(4):1774–1793
2. Agency for Healthcare Research and Quality. Management of Bronchiolitis in Infants and Children. Evidence Report/Technology Assessment No. 69. Rockville, MD: Agency for Healthcare Research and Quality; 2003. AHRQ Publication No. 03-E014
3. Mullins JA, Lamonte AC, Bresee JS, Anderson LJ. Substantial variability in community respiratory syncytial virus season timing. *Pediatr Infect Dis J*. 2003; 22(10):857–862
4. Centers for Disease Control and Prevention. Respiratory syncytial virus activity—United States, July 2011–January 2013. *MMWR Morb Mortal Wkly Rep*. 2013; 62(8):141–144
5. Greenough A, Cox S, Alexander J, et al. Health care utilisation of infants with chronic lung disease, related to hospitalisation for RSV infection. *Arch Dis Child*. 2001;85(6):463–468
6. Parrott RH, Kim HW, Arrobio JO, et al. Epidemiology of respiratory syncytial virus infection in Washington, D.C. II. Infection and disease with respect to age, immunologic status, race and sex. *Am J Epidemiol*. 1973;98(4):289–300
7. Meissner HC. Selected populations at increased risk from respiratory syncytial virus infection. *Pediatr Infect Dis J*. 2003; 22(suppl 2):S40–S44, discussion S44–S45
8. Shay DK, Holman RC, Roosevelt GE, Clarke MJ, Anderson LJ. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979–1997. *J Infect Dis*. 2001; 183(1):16–22
9. Miller EK, Gebretsadik T, Carroll KN, et al. Viral etiologies of infant bronchiolitis, croup and upper respiratory illness during 4 consecutive years. *Pediatr Infect Dis J*. 2013;32(9):950–955
10. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA Jr. Trends in bronchiolitis hospitalizations in the United States, 2000–2009. *Pediatrics*. 2013;132(1): 28–36
11. Hall CB, Weinberg GA, Blumkin AK, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. *Pediatrics*. 2013; 132(2). Available at: www.pediatrics.org/cgi/content/full/132/2/e341
12. Hall CB. Nosocomial respiratory syncytial virus infections: the “Cold War” has not ended. *Clin Infect Dis*. 2000;31(2): 590–596
13. Stevens TP, Sinkin RA, Hall CB, Maniscalco WM, McConnochie KM. Respiratory syncytial virus and premature infants born at 32 weeks’ gestation or earlier: hospitalization and economic implications of prophylaxis. *Arch Pediatr Adolesc Med*. 2000; 154(1):55–61
14. American Academy of Pediatrics Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics*. 2004;114(3):874–877

15. Ricart S, Marcos MA, Sarda M, et al. Clinical risk factors are more relevant than respiratory viruses in predicting bronchiolitis severity. *Pediatr Pulmonol*. 2013;48(5):456–463
16. Shaw KN, Bell LM, Sherman NH. Outpatient assessment of infants with bronchiolitis. *Am J Dis Child*. 1991;145(2):151–155
17. Hall CB, Powell KR, MacDonald NE, et al. Respiratory syncytial viral infection in children with compromised immune function. *N Engl J Med*. 1986;315(2):77–81
18. Mansbach JM, Piedra PA, Stevenson MD, et al; MARC-30 Investigators. Prospective multicenter study of children with bronchiolitis requiring mechanical ventilation. *Pediatrics*. 2012;130(3). Available at: www.pediatrics.org/cgi/content/full/130/3/e492
19. Prescott WA Jr, Hutchinson DJ. Respiratory syncytial virus prophylaxis in special populations: is it something worth considering in cystic fibrosis and immunosuppression? *J Pediatr Pharmacol Ther*. 2011;16(2):77–86
20. Armstrong D, Grimwood K, Carlin JB, et al. Severe viral respiratory infections in infants with cystic fibrosis. *Pediatr Pulmonol*. 1998;26(6):371–379
21. Alvarez AE, Marson FA, Bertuzzo CS, Arns CW, Ribeiro JD. Epidemiological and genetic characteristics associated with the severity of acute viral bronchiolitis by respiratory syncytial virus. *J Pediatr (Rio J)*. 2013;89(6):531–543
22. Iliff A, Lee VA. Pulse rate, respiratory rate, and body temperature of children between two months and eighteen years of age. *Child Dev*. 1952;23(4):237–245
23. Rogers MC. Respiratory monitoring. In: Rogers MC, Nichols DG, eds. *Textbook of Pediatric Intensive Care*. Baltimore, MD: Williams & Wilkins; 1996:332–333
24. Berman S, Simoes EA, Lanata C. Respiratory rate and pneumonia in infancy. *Arch Dis Child*. 1991;66(1):81–84
25. Fleming S, Thompson M, Stevens R, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. *Lancet*. 2011;377(9770):1011–1018
26. Bonafide CP, Brady PW, Keren R, Conway PH, Marsolo K, Daymont C. Development of heart and respiratory rate percentile curves for hospitalized children. *Pediatrics*. 2013;131(4). Available at: www.pediatrics.org/cgi/content/full/131/4/e1150
27. Margolis P, Gadomski A. The rational clinical examination. Does this infant have pneumonia? *JAMA*. 1998;279(4):308–313
28. Mahabee-Gittens EM, Grupp-Phelan J, Brody AS, et al. Identifying children with pneumonia in the emergency department. *Clin Pediatr (Phila)*. 2005;44(5):427–435
29. Brooks AM, McBride JT, McConnochie KM, Aviram M, Long C, Hall CB. Predicting deterioration in previously healthy infants hospitalized with respiratory syncytial virus infection. *Pediatrics*. 1999;104(3 pt 1):463–467
30. Neuman MI, Monuteaux MC, Scully KJ, Bachur RG. Prediction of pneumonia in a pediatric emergency department. *Pediatrics*. 2011;128(2):246–253
31. Shah S, Bachur R, Kim D, Neuman MI. Lack of predictive value of tachypnea in the diagnosis of pneumonia in children. *Pediatr Infect Dis J*. 2010;29(5):406–409
32. Mansbach JM, McAdam AJ, Clark S, et al. Prospective multicenter study of the viral etiology of bronchiolitis in the emergency department. *Acad Emerg Med*. 2008;15(2):111–118
33. Mansbach JM, Piedra PA, Teach SJ, et al; MARC-30 Investigators. Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis. *Arch Pediatr Adolesc Med*. 2012;166(8):700–706
34. Navas L, Wang E, de Carvalho V, Robinson J; Pediatric Investigators Collaborative Network on Infections in Canada. Improved outcome of respiratory syncytial virus infection in a high-risk hospitalized population of Canadian children. *J Pediatr*. 1992;121(3):348–354
35. Wang EE, Law BJ, Stephens D. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr*. 1995;126(2):212–219
36. Chan PW, Lok FY, Khatijah SB. Risk factors for hypoxemia and respiratory failure in respiratory syncytial virus bronchiolitis. *Southeast Asian J Trop Med Public Health*. 2002;33(4):806–810
37. Roback MG, Baskin MN. Failure of oxygen saturation and clinical assessment to predict which patients with bronchiolitis discharged from the emergency department will return requiring admission. *Pediatr Emerg Care*. 1997;13(1):9–11
38. Lowell DI, Lister G, Von Koss H, McCarthy P. Wheezing in infants: the response to epinephrine. *Pediatrics*. 1987;79(6):939–945
39. Destino L, Weisgerber MC, Soung P, et al. Validity of respiratory scores in bronchiolitis. *Hosp Pediatr*. 2012;2(4):202–209
40. Schroeder AR, Marmor AK, Pantell RH, Newman TB. Impact of pulse oximetry and oxygen therapy on length of stay in bronchiolitis hospitalizations. *Arch Pediatr Adolesc Med*. 2004;158(6):527–530
41. Dawson KP, Long A, Kennedy J, Mogridge N. The chest radiograph in acute bronchiolitis. *J Paediatr Child Health*. 1990;26(4):209–211
42. Schroeder AR, Mansbach JM, Stevenson M, et al. Apnea in children hospitalized with bronchiolitis. *Pediatrics*. 2013;132(5). Available at: www.pediatrics.org/cgi/content/full/132/5/e1194
43. Ralston S, Hill V. Incidence of apnea in infants hospitalized with respiratory syncytial virus bronchiolitis: a systematic review. *J Pediatr*. 2009;155(5):728–733
44. Willwerth BM, Harper MB, Greenes DS. Identifying hospitalized infants who have bronchiolitis and are at high risk for apnea. *Ann Emerg Med*. 2006;48(4):441–447
45. García CG, Bhoré R, Soriano-Fallas A, et al. Risk factors in children hospitalized with RSV bronchiolitis versus non-RSV bronchiolitis. *Pediatrics*. 2010;126(6). Available at: www.pediatrics.org/cgi/content/full/126/6/e1453
46. Swingler GH, Hussey GD, Zwarenstein M. Randomised controlled trial of clinical outcome after chest radiograph in ambulatory acute lower-respiratory infection in children. *Lancet*. 1998;351(9100):404–408
47. Schuh S, Lalani A, Allen U, et al. Evaluation of the utility of radiography in acute bronchiolitis. *J Pediatr*. 2007;150(4):429–433
48. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Efficacy of bronchodilator therapy in bronchiolitis. A meta-analysis. *Arch Pediatr Adolesc Med*. 1996;150(11):1166–1172
49. Flores G, Horwitz RI. Efficacy of beta2-agonists in bronchiolitis: a reappraisal and meta-analysis. *Pediatrics*. 1997;100(2 pt 1):233–239
50. Hartling L, Wiebe N, Russell K, Patel H, Klassen TP. A meta-analysis of randomized controlled trials evaluating the efficacy of epinephrine for the treatment of acute viral bronchiolitis. *Arch Pediatr Adolesc Med*. 2003;157(10):957–964
51. King VJ, Viswanathan M, Bordley WC, et al. Pharmacologic treatment of bronchiolitis in infants and children: a systematic review. *Arch Pediatr Adolesc Med*. 2004;158(2):127–137
52. Zorc JJ, Hall CB. Bronchiolitis: recent evidence on diagnosis and management. *Pediatrics*. 2010;125(2):342–349
53. Wainwright C. Acute viral bronchiolitis in children—a very common condition with few therapeutic options. *Paediatr Respir Rev*. 2010;11(1):39–45, quiz 45

54. Walsh P, Caldwell J, McQuillan KK, Friese S, Robbins D, Rothenberg SJ. Comparison of nebulized epinephrine to albuterol in bronchiolitis. *Acad Emerg Med*. 2008;15(4):305–313
55. Scarlett EE, Walker S, Rovitelli A, Ren CL. Tidal breathing responses to albuterol and normal saline in infants with viral bronchiolitis. *Pediatr Allergy Immunol Pulmonol*. 2012;25(4):220–225
56. Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev*. 2014;(6):CD001266
57. Mallol J, Barrueto L, Girardi G, et al. Use of nebulized bronchodilators in infants under 1 year of age: analysis of four forms of therapy. *Pediatr Pulmonol*. 1987;3(5):298–303
58. Lines DR, Kattampallil JS, Liston P. Efficacy of nebulized salbutamol in bronchiolitis. *Pediatr Rev Commun*. 1990;5(2):121–129
59. Alario AJ, Lewander WJ, Dennehy P, Seifer R, Mansell AL. The efficacy of nebulized metaproterenol in wheezing infants and young children. *Am J Dis Child*. 1992;146(4):412–418
60. Chavasse RJPG, Seddon P, Bara A, McKean MC. Short acting beta2-agonists for recurrent wheeze in children under two years of age. *Cochrane Database Syst Rev*. 2009;(2):CD002873
61. Totapally BR, Demerci C, Zureikat G, Nolan B. Tidal breathing flow-volume loops in bronchiolitis in infancy: the effect of albuterol [ISRCTN47364493]. *Crit Care*. 2002;6(2):160–165
62. Levin DL, Garg A, Hall LJ, Slogic S, Jarvis JD, Leiter JC. A prospective randomized controlled blinded study of three bronchodilators in infants with respiratory syncytial virus bronchiolitis on mechanical ventilation. *Pediatr Crit Care Med*. 2008;9(6):598–604
63. Bjornson C, Russell K, Vandermeer B, Klassen TP, Johnson DW. Nebulized epinephrine for croup in children. *Cochrane Database Syst Rev*. 2013;(10):CD006619
64. Hartling L, Fernandes RM, Bialy L, et al. Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis. *BMJ*. 2011;342:d1714
65. Wainwright C, Altamirano L, Cheney M, et al. A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. *N Engl J Med*. 2003;349(1):27–35
66. Patel H, Gouin S, Platt RW. Randomized, double-blind, placebo-controlled trial of oral albuterol in infants with mild-to-moderate acute viral bronchiolitis. *J Pediatr*. 2003;142(5):509–514
67. Skjerven HO, Hunderi JO, Brüggmann-Pieper SK, et al. Racemic adrenaline and inhalation strategies in acute bronchiolitis. *N Engl J Med*. 2013;368(24):2286–2293
68. Plint AC, Johnson DW, Patel H, et al; Pediatric Emergency Research Canada (PERC). Epinephrine and dexamethasone in children with bronchiolitis. *N Engl J Med*. 2009;360(20):2079–2089
69. Wark PA, McDonald V, Jones AP. Nebulised hypertonic saline for cystic fibrosis. *Cochrane Database Syst Rev*. 2005;(3):CD001506
70. Daviskas E, Anderson SD, Gonda I, et al. Inhalation of hypertonic saline aerosol enhances mucociliary clearance in asthmatic and healthy subjects. *Eur Respir J*. 1996;9(4):725–732
71. Sood N, Bennett WD, Zeman K, et al. Increasing concentration of inhaled saline with or without amiloride: effect on mucociliary clearance in normal subjects. *Am J Respir Crit Care Med*. 2003;167(2):158–163
72. Mandelberg A, Amirav I. Hypertonic saline or high volume normal saline for viral bronchiolitis: mechanisms and rationale. *Pediatr Pulmonol*. 2010;45(1):36–40
73. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulized hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst Rev*. 2008;(4):CD006458
74. Jacobs JD, Foster M, Wan J, Pershad J. 7% Hypertonic saline in acute bronchiolitis: a randomized controlled trial. *Pediatrics*. 2014;133(1). Available at: www.pediatrics.org/cgi/content/full/133/1/e8
75. Wu S, Baker C, Lang ME, et al. Nebulized hypertonic saline for bronchiolitis: a randomized clinical trial. *JAMA Pediatr*. 2014;168(7):657–663
76. Florin TA, Shaw KN, Kittick M, Yakscoe S, Zorc JJ. Nebulized hypertonic saline for bronchiolitis in the emergency department: a randomized clinical trial. *JAMA Pediatr*. 2014;168(7):664–670
77. Sharma BS, Gupta MK, Rafik SP. Hypertonic (3%) saline vs 0.93% saline nebulization for acute viral bronchiolitis: a randomized controlled trial. *Indian Pediatr*. 2013;50(8):743–747
78. Silver AH. Randomized controlled trial of the efficacy of nebulized 3% saline without bronchodilators for infants admitted with bronchiolitis: preliminary data [abstr E-PAS2014:2952.685]. Paper presented at: Pediatric Academic Societies Annual Meeting; May 3–6, 2014; Vancouver, British Columbia, Canada
79. Ralston S, Hill V, Martinez M. Nebulized hypertonic saline without adjunctive bronchodilators for children with bronchiolitis. *Pediatrics*. 2010;126(3). Available at: www.pediatrics.org/cgi/content/full/126/3/e520
80. Luo Z, Liu E, Luo J, et al. Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. *Pediatr Int*. 2010;52(2):199–202
81. Sarrell EM, Tal G, Witzling M, et al. Nebulized 3% hypertonic saline solution treatment in ambulatory children with viral bronchiolitis decreases symptoms. *Chest*. 2002;122(6):2015–2020
82. Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev*. 2001;(1):CD002178
83. Smith M, Iqbal S, Elliott TM, Everard M, Rowe BH. Corticosteroids for hospitalised children with acute asthma. *Cochrane Database Syst Rev*. 2003;(2):CD002886
84. Russell KF, Liang Y, O'Gorman K, Johnson DW, Klassen TP. Glucocorticoids for croup. *Cochrane Database Syst Rev*. 2011;(1):CD001955
85. Fernandes RM, Bialy LM, Vandermeer B, et al. Glucocorticoids for acute viral bronchiolitis in infants and young children. *Cochrane Database Syst Rev*. 2013;(6):CD004878
86. Corneli HM, Zorc JJ, Mahajan P, et al; Bronchiolitis Study Group of the Pediatric Emergency Care Applied Research Network (PECARN). A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis [published correction appears in *N Engl J Med* 2008;359(18):1972]. *N Engl J Med*. 2007;357(4):331–339
87. Frey U, von Mutius E. The challenge of managing wheezing in infants. *N Engl J Med*. 2009;360(20):2130–2133
88. Gibson PG, Powell H, Ducharme F. Long-acting beta2-agonists as an inhaled corticosteroid-sparing agent for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2005;(4):CD005076
89. Barnes PJ. Scientific rationale for using a single inhaler for asthma control. *Eur Respir J*. 2007;29(3):587–595
90. Giembycz MA, Kaur M, Leigh R, Newton R. A Holy Grail of asthma management: toward understanding how long-acting beta (2)-adrenoceptor agonists enhance the clinical efficacy of inhaled corticosteroids. *Br J Pharmacol*. 2008;153(6):1090–1104
91. Kaur M, Chivers JE, Giembycz MA, Newton R. Long-acting beta2-adrenoceptor agonists synergistically enhance glucocorticoid-dependent transcription in human airway

- epithelial and smooth muscle cells. *Mol Pharmacol*. 2008;73(1):203–214
92. Holden NS, Bell MJ, Rider CF, et al. β 2-Adrenoceptor agonist-induced RGS2 expression is a genomic mechanism of bronchoprotection that is enhanced by glucocorticoids. *Proc Natl Acad Sci U S A*. 2011;108(49):19713–19718
 93. Schuh S, Coates AL, Binnie R, et al. Efficacy of oral dexamethasone in outpatients with acute bronchiolitis. *J Pediatr*. 2002;140(1):27–32
 94. Bentur L, Shoseyov D, Feigenbaum D, Gorichovsky Y, Bibi H. Dexamethasone inhalations in RSV bronchiolitis: a double-blind, placebo-controlled study. *Acta Paediatr*. 2005;94(7):866–871
 95. Kuyucu S, Unal S, Kuyucu N, Yilgor E. Additive effects of dexamethasone in nebulized salbutamol or L-epinephrine treated infants with acute bronchiolitis. *Pediatr Int*. 2004;46(5):539–544
 96. Mesquita M, Castro-Rodríguez JA, Heinichen L, Fariña E, Iramain R. Single oral dose of dexamethasone in outpatients with bronchiolitis: a placebo controlled trial. *Allergol Immunopathol (Madr)*. 2009;37(2):63–67
 97. Alansari K, Sakran M, Davidson BL, Ibrahim K, Alrefai M, Zakaria I. Oral dexamethasone for bronchiolitis: a randomized trial. *Pediatrics*. 2013;132(4). Available at: www.pediatrics.org/cgi/content/full/132/4/e810
 98. Mallory MD, Shay DK, Garrett J, Bordley WC. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. *Pediatrics*. 2003;111(1). Available at: www.pediatrics.org/cgi/content/full/111/1/e45
 99. Corneli HM, Zorc JJ, Holubkov R, et al; Bronchiolitis Study Group for the Pediatric Emergency Care Applied Research Network. Bronchiolitis: clinical characteristics associated with hospitalization and length of stay. *Pediatr Emerg Care*. 2012;28(2):99–103
 100. Unger S, Cunningham S. Effect of oxygen supplementation on length of stay for infants hospitalized with acute viral bronchiolitis. *Pediatrics*. 2008;121(3):470–475
 101. Cunningham S, McMurray A. Observational study of two oxygen saturation targets for discharge in bronchiolitis. *Arch Dis Child*. 2012;97(4):361–363
 102. Anaesthesia UK. Oxygen dissociation curve. Available at: [http://www.anaesthesiauk.com/SearchRender.aspx?DocId=1419&Index=D%3a\dtSearch\UserData\AUK&HitCount=](http://www.anaesthesiauk.com/SearchRender.aspx?DocId=1419&Index=D%3a\dtSearch\UserData\AUK&HitCount=19&hits=4+5+d+e+23+24+37+58+59+a7+a8+14a+14b+17e+180+181+1a9+1aa+1d4)
 103. McBride SC, Chiang VW, Goldmann DA, Landrigan CP. Preventable adverse events in infants hospitalized with bronchiolitis. *Pediatrics*. 2005;116(3):603–608
 104. Hunt CE, Corwin MJ, Lister G, et al; Collaborative Home Infant Monitoring Evaluation (CHIME) Study Group. Longitudinal assessment of hemoglobin oxygen saturation in healthy infants during the first 6 months of age. *J Pediatr*. 1999;135(5):580–586
 105. Gavlak JC, Stocks J, Laverty A, et al. The Young Everest Study: preliminary report of changes in sleep and cerebral blood flow velocity during slow ascent to altitude in unacclimatised children. *Arch Dis Child*. 2013;98(5):356–362
 106. O'Neil SL, Barysh N, Setear SJ. Determining school programming needs of special population groups: a study of asthmatic children. *J Sch Health*. 1985;55(6):237–239
 107. Bender BG, Belleau L, Fukuhara JT, Mrazek DA, Strunk RC. Psychomotor adaptation in children with severe chronic asthma. *Pediatrics*. 1987;79(5):723–727
 108. Rietveld S, Colland VT. The impact of severe asthma on schoolchildren. *J Asthma*. 1999;36(5):409–417
 109. Sung V, Massie J, Hochmann MA, Carlin JB, Jansen K, Robertson CF. Estimating inspired oxygen concentration delivered by nasal prongs in children with bronchiolitis. *J Paediatr Child Health*. 2008;44(1-2):14–18
 110. Ross PA, Newth CJL, Khemani RG. Accuracy of pulse oximetry in children. *Pediatrics*. 2014;133(1):22–29
 111. Hasselbalch KA. Neutralitätsregulation und reizbarkeit des atemzentrums in ihren Wirkungen auf die koklensaurespannung des Blutes. *Biochem Ztschr*. 1912;46:403–439
 112. Wang EE, Milner RA, Navas L, Maj H. Observer agreement for respiratory signs and oximetry in infants hospitalized with lower respiratory infections. *Am Rev Respir Dis*. 1992;145(1):106–109
 113. Rojas MX, Granados Rugeles C, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. *Cochrane Database Syst Rev*. 2009;(1):CD005975
 114. Mitka M. Joint commission warns of alarm fatigue: multitude of alarms from monitoring devices problematic. *JAMA*. 2013;309(22):2315–2316
 115. Bowton DL, Scuderi PE, Harris L, Haponik EF. Pulse oximetry monitoring outside the intensive care unit: progress or problem? *Ann Intern Med*. 1991;115(6):450–454
 116. Groothuis JR, Gutierrez KM, Lauer BA. Respiratory syncytial virus infection in children with bronchopulmonary dysplasia. *Pediatrics*. 1988;82(2):199–203
 117. Voepel-Lewis T, Pechlavanidis E, Burke C, Talsma AN. Nursing surveillance moderates the relationship between staffing levels and pediatric postoperative serious adverse events: a nested case-control study. *Int J Nurs Stud*. 2013;50(7):905–913
 118. Bajaj L, Turner CG, Bothner J. A randomized trial of home oxygen therapy from the emergency department for acute bronchiolitis. *Pediatrics*. 2006;117(3):633–640
 119. Tie SW, Hall GL, Peter S, et al. Home oxygen for children with acute bronchiolitis. *Arch Dis Child*. 2009;94(8):641–643
 120. Halstead S, Roosevelt G, Deakynne S, Bajaj L. Discharged on supplemental oxygen from an emergency department in patients with bronchiolitis. *Pediatrics*. 2012;129(3). Available at: www.pediatrics.org/cgi/content/full/129/3/e605
 121. Sandweiss DR, Mundorff MB, Hill T, et al. Decreasing hospital length of stay for bronchiolitis by using an observation unit and home oxygen therapy. *JAMA Pediatr*. 2013;167(5):422–428
 122. Flett KB, Breslin K, Braun PA, Hambidge SJ. Outpatient course and complications associated with home oxygen therapy for mild bronchiolitis. *Pediatrics*. 2014;133(5):769–775
 123. Gauthier M, Vincent M, Morneau S, Chevalier I. Impact of home oxygen therapy on hospital stay for infants with acute bronchiolitis. *Eur J Pediatr*. 2012;171(12):1839–1844
 124. Bergman AB. Pulse oximetry: good technology misapplied. *Arch Pediatr Adolesc Med*. 2004;158(6):594–595
 125. Sandweiss DR, Kadish HA, Campbell KA. Outpatient management of patients with bronchiolitis discharged home on oxygen: a survey of general pediatricians. *Clin Pediatr (Phila)*. 2012;51(5):442–446
 126. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. *Respir Med*. 2009;103(10):1400–1405
 127. Milési C, Baleine J, Matecki S, et al. Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A physiologic study [published correction appears in *Intensive Care Med*. 2013;39(6):1170]. *Intensive Care Med*. 2013;39(6):1088–1094

128. Arora B, Mahajan P, Zidan MA, Sethuraman U. Nasopharyngeal airway pressures in bronchiolitis patients treated with high-flow nasal cannula oxygen therapy. *Pediatr Emerg Care*. 2012;28(11):1179–1184
129. Spentzas T, Minarik M, Patters AB, Vinson B, Stidham G. Children with respiratory distress treated with high-flow nasal cannula. *J Intensive Care Med*. 2009;24(5):323–328
130. Hegde S, Prodhan P. Serious air leak syndrome complicating high-flow nasal cannula therapy: a report of 3 cases. *Pediatrics*. 2013;131(3). Available at: www.pediatrics.org/cgi/content/full/131/3/e939
131. Pham TM, O'Malley L, Mayfield S, Martin S, Schibler A. The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis [published online ahead of print May 21, 2014]. *Pediatr Pulmonol*. doi:10.1002/ppul.23060
132. Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. *Eur J Pediatr*. 2013;172(12):1649–1656
133. Ganu SS, Gautam A, Wilkins B, Egan J. Increase in use of non-invasive ventilation for infants with severe bronchiolitis is associated with decline in intubation rates over a decade. *Intensive Care Med*. 2012;38(7):1177–1183
134. Wing R, James C, Maranda LS, Armsby CC. Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. *Pediatr Emerg Care*. 2012;28(11):1117–1123
135. McKiernan C, Chua LC, Visintainer PF, Allen H. High flow nasal cannulae therapy in infants with bronchiolitis. *J Pediatr*. 2010;156(4):634–638
136. Schibler A, Pham TM, Dunster KR, et al. Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. *Intensive Care Med*. 2011;37(5):847–852
137. Kelly GS, Simon HK, Sturm JJ. High-flow nasal cannula use in children with respiratory distress in the emergency department: predicting the need for subsequent intubation. *Pediatr Emerg Care*. 2013;29(8):888–892
138. Kallappa C, Hufton M, Millen G, Ninan TK. Use of high flow nasal cannula oxygen (HFNCO) in infants with bronchiolitis on a paediatric ward: a 3-year experience. *Arch Dis Child*. 2014;99(8):790–791
139. Hilliard TN, Archer N, Laura H, et al. Pilot study of vapotherm oxygen delivery in moderately severe bronchiolitis. *Arch Dis Child*. 2012;97(2):182–183
140. Roqué i Figuls M, Giné-Garriga M, Granados Rugeles C, Perrotta C. Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. *Cochrane Database Syst Rev*. 2012;(2):CD004873
141. Aviram M, Damri A, Yekutielli C, Bearman J, Tal A. Chest physiotherapy in acute bronchiolitis [abstract]. *Eur Respir J*. 1992;5(suppl 15):229–230
142. Webb MS, Martin JA, Cartlidge PH, Ng YK, Wright NA. Chest physiotherapy in acute bronchiolitis. *Arch Dis Child*. 1985;60(11):1078–1079
143. Nicholas KJ, Dhouieb MO, Marshal TG, Edmunds AT, Grant MB. An evaluation of chest physiotherapy in the management of acute bronchiolitis: changing clinical practice. *Physiotherapy*. 1999;85(12):669–674
144. Bohé L, Ferrero ME, Cuestas E, Polliotto L, Genoff M. Indications of conventional chest physiotherapy in acute bronchiolitis [in Spanish]. *Medicina (B Aires)*. 2004;64(3):198–200
145. De Córdoba F, Rodrigues M, Luque A, Cadrobbi C, Faria R, Solé D. Fisioterapia respiratória em lactentes com bronquiólite: realizar ou não? *Mundo Saúde*. 2008;32(2):183–188
146. Gajdos V, Katsahian S, Beydon N, et al. Effectiveness of chest physiotherapy in infants hospitalized with acute bronchiolitis: a multicenter, randomized, controlled trial. *PLoS Med*. 2010;7(9):e1000345
147. Rochat I, Leis P, Bouchardy M, et al. Chest physiotherapy using passive expiratory techniques does not reduce bronchiolitis severity: a randomised controlled trial. *Eur J Pediatr*. 2012;171(3):457–462
148. Postiaux G, Louis J, Labasse HC, et al. Evaluation of an alternative chest physiotherapy method in infants with respiratory syncytial virus bronchiolitis. *Respir Care*. 2011;56(7):989–994
149. Sánchez Bayle M, Martín Martín R, Cano Fernández J, et al. Chest physiotherapy and bronchiolitis in the hospitalised infant. Double-blind clinical trial [in Spanish]. *An Pediatr (Barc)*. 2012;77(1):5–11
150. Mussman GM, Parker MW, Statile A, Sucharew H, Brady PW. Suctioning and length of stay in infants hospitalized with bronchiolitis. *JAMA Pediatr*. 2013;167(5):414–421
151. Weisgerber MC, Lye PS, Li SH, et al. Factors predicting prolonged hospital stay for infants with bronchiolitis. *J Hosp Med*. 2011;6(5):264–270
152. Nichol KP, Cherry JD. Bacterial-viral interrelations in respiratory infections of children. *N Engl J Med*. 1967;277(13):667–672
153. Field CM, Connolly JH, Murtagh G, Slattery CM, Turkington EE. Antibiotic treatment of epidemic bronchiolitis—a double-blind trial. *BMJ*. 1966;1(5479):83–85
154. Antonow JA, Hansen K, McKinstry CA, Byington CL. Sepsis evaluations in hospitalized infants with bronchiolitis. *Pediatr Infect Dis J*. 1998;17(3):231–236
155. Friis B, Andersen P, Brenøe E, et al. Antibiotic treatment of pneumonia and bronchiolitis. A prospective randomised study. *Arch Dis Child*. 1984;59(11):1038–1045
156. Greenes DS, Harper MB. Low risk of bacteremia in febrile children with recognizable viral syndromes. *Pediatr Infect Dis J*. 1999;18(3):258–261
157. Spurling GK, Doust J, Del Mar CB, Eriksson L. Antibiotics for bronchiolitis in children. *Cochrane Database Syst Rev*. 2011;(6):CD005189
158. Ralston S, Hill V, Waters A. Occult serious bacterial infection in infants younger than 60 to 90 days with bronchiolitis: a systematic review. *Arch Pediatr Adolesc Med*. 2011;165(10):951–956
159. Purcell K, Fergie J. Lack of usefulness of an abnormal white blood cell count for predicting a concurrent serious bacterial infection in infants and young children hospitalized with respiratory syncytial virus lower respiratory tract infection. *Pediatr Infect Dis J*. 2007;26(4):311–315
160. Purcell K, Fergie J. Concurrent serious bacterial infections in 2396 infants and children hospitalized with respiratory syncytial virus lower respiratory tract infections. *Arch Pediatr Adolesc Med*. 2002;156(4):322–324
161. Purcell K, Fergie J. Concurrent serious bacterial infections in 912 infants and children hospitalized for treatment of respiratory syncytial virus lower respiratory tract infection. *Pediatr Infect Dis J*. 2004;23(3):267–269
162. Kuppermann N, Bank DE, Walton EA, Senac MO Jr, McCaslin I. Risks for bacteremia and urinary tract infections in young febrile children with bronchiolitis. *Arch Pediatr Adolesc Med*. 1997;151(12):1207–1214
163. Titus MO, Wright SW. Prevalence of serious bacterial infections in febrile infants with respiratory syncytial virus infection. *Pediatrics*. 2003;112(2):282–284
164. Melendez E, Harper MB. Utility of sepsis evaluation in infants 90 days of age or younger with fever and clinical bronchiolitis. *Pediatr Infect Dis J*. 2003;22(12):1053–1056
165. Hall CB, Powell KR, Schnabel KC, Gala CL, Pincus PH. Risk of secondary bacterial

- infection in infants hospitalized with respiratory syncytial viral infection. *J Pediatr*. 1988;113(2):266–271
166. Hall CB. Respiratory syncytial virus: a continuing culprit and conundrum. *J Pediatr*. 1999;135(2 pt 2):2–7
 167. Davies HD, Matlow A, Petric M, Glazier R, Wang EE. Prospective comparative study of viral, bacterial and atypical organisms identified in pneumonia and bronchiolitis in hospitalized Canadian infants. *Pediatr Infect Dis J*. 1996;15(4):371–375
 168. Levine DA, Platt SL, Dayan PS, et al; Multicenter RSV-SBI Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections. *Pediatrics*. 2004;113(6):1728–1734
 169. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev*. 2000;(2):CD001266
 170. Pinto LA, Pitrez PM, Luisi F, et al. Azithromycin therapy in hospitalized infants with acute bronchiolitis is not associated with better clinical outcomes: a randomized, double-blinded, and placebo-controlled clinical trial. *J Pediatr*. 2012;161(6):1104–1108
 171. McCallum GB, Morris PS, Chang AB. Antibiotics for persistent cough or wheeze following acute bronchiolitis in children. *Cochrane Database Syst Rev*. 2012;(12):CD009834
 172. Levin D, Tribuzio M, Green-Wrzesinski T, et al. Empiric antibiotics are justified for infants with RSV presenting with respiratory failure. *Pediatr Crit Care*. 2010;11(3):390–395
 173. Thorburn K, Reddy V, Taylor N, van Saene HK. High incidence of pulmonary bacterial co-infection in children with severe respiratory syncytial virus (RSV) bronchiolitis. *Thorax*. 2006;61(7):611–615
 174. Gomaa MA, Galal O, Mahmoud MS. Risk of acute otitis media in relation to acute bronchiolitis in children. *Int J Pediatr Otorhinolaryngol*. 2012;76(1):49–51
 175. Andrade MA, Hoberman A, Glustein J, Paradise JL, Wald ER. Acute otitis media in children with bronchiolitis. *Pediatrics*. 1998;101(4 pt 1):617–619
 176. Shazberg G, Revel-Vilk S, Shoseyov D, Ben-Ami A, Klar A, Hurvitz H. The clinical course of bronchiolitis associated with acute otitis media. *Arch Dis Child*. 2000;83(4):317–319
 177. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media [published correction appears in *Pediatrics*. 2014;133(2):346]. *Pediatrics*. 2013;131(3). Available at: www.pediatrics.org/cgi/content/full/131/3/e964
 178. Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. *N Engl J Med*. 2011;364(2):105–115
 179. Tähtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. *N Engl J Med*. 2011;364(2):116–126
 180. Corrad F, de La Rocque F, Martin E, et al. Food intake during the previous 24 h as a percentage of usual intake: a marker of hypoxia in infants with bronchiolitis: an observational, prospective, multicenter study. *BMC Pediatr*. 2013;13:6
 181. Pinnington LL, Smith CM, Ellis RE, Morton RE. Feeding efficiency and respiratory integration in infants with acute viral bronchiolitis. *J Pediatr*. 2000;137(4):523–526
 182. Khoshoo V, Edell D. Previously healthy infants may have increased risk of aspiration during respiratory syncytial viral bronchiolitis. *Pediatrics*. 1999;104(6):1389–1390
 183. Kennedy N, Flanagan N. Is nasogastric fluid therapy a safe alternative to the intravenous route in infants with bronchiolitis? *Arch Dis Child*. 2005;90(3):320–321
 184. Sammartino L, James D, Goutzamanis J, Lines D. Nasogastric rehydration does have a role in acute paediatric bronchiolitis. *J Paediatr Child Health*. 2002;38(3):321–322
 185. Kugelman A, Raibin K, Dabbah H, et al. Intravenous fluids versus gastric-tube feeding in hospitalized infants with viral bronchiolitis: a randomized, prospective pilot study. *J Pediatr*. 2013;162(3):640–642. e1
 186. Oakley E, Borland M, Neutze J, et al; Paediatric Research in Emergency Departments International Collaborative (PREDICT). Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial. *Lancet Respir Med*. 2013;1(2):113–120
 187. Gozal D, Colin AA, Jaffe M, Hochberg Z. Water, electrolyte, and endocrine homeostasis in infants with bronchiolitis. *Pediatr Res*. 1990;27(2):204–209
 188. van Steensel-Moll HA, Hazelzet JA, van der Voort E, Neijens HJ, Hackeng WH. Excessive secretion of antidiuretic hormone in infections with respiratory syncytial virus. *Arch Dis Child*. 1990;65(11):1237–1239
 189. Rivers RP, Forsling ML, Olver RP. Inappropriate secretion of antidiuretic hormone in infants with respiratory infections. *Arch Dis Child*. 1981;56(5):358–363
 190. Wang J, Xu E, Xiao Y. Isotonic versus hypotonic maintenance IV fluids in hospitalized children: a meta-analysis. *Pediatrics*. 2014;133(1):105–113
 191. American Academy of Pediatrics, Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Policy statement: updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014;134(2):415–420
 192. American Academy of Pediatrics; Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Technical report: updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014;134(2):e620–e638.
 193. IMPact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. The IMPact-RSV Study Group. *Pediatrics*. 1998;102(3):531–537
 194. Feltes TF, Cabalk AK, Meissner HC, et al. Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr*. 2003;143(4):532–540
 195. Andabaka T, Nickerson JW, Rojas-Reyes MX, Rueda JD, Bacic VV, Barsic B. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. *Cochrane Database Syst Rev*. 2013;(4):CD006602
 196. Wang D, Bayliss S, Meads C. Palivizumab for immunoprophylaxis of respiratory syncytial virus (RSV) bronchiolitis in high-risk infants and young children: a systematic review and additional economic modelling of subgroup analyses. *Health Technol Assess*. 2011;1(5):iii–iv, 1–124
 197. Hampf C, Kauf TL, Saidi AS, Winterstein AG. Cost-effectiveness of respiratory syncytial virus prophylaxis in various indications. *Arch Pediatr Adolesc Med*. 2011;165(6):498–505
 198. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. *N Engl J Med*. 2009;360(6):588–598
 199. Dupenthaler A, Ammann RA, Gorgievski-Hrisoho M, et al. Low incidence of respiratory syncytial virus hospitalisations in haemodynamically significant congenital

- heart disease. *Arch Dis Child*. 2004;89:961–965
200. Geskey JM, Thomas NJ, Brummel GL. Palivizumab in congenital heart disease: should international guidelines be revised? *Expert Opin Biol Ther*. 2007;7(11):1615–1620
 201. Robbie GJ, Zhao L, Mondick J, Losonsky G, Roskos LK. Population pharmacokinetics of palivizumab, a humanized anti-respiratory syncytial virus monoclonal antibody, in adults and children. *Anti-microb Agents Chemother*. 2012;56(9):4927–4936
 202. Megged O, Schlesinger Y. Down syndrome and respiratory syncytial virus infection. *Pediatr Infect Dis J*. 2010;29(7):672–673
 203. Robinson KA, Odelola OA, Saldanha IJ, Mckoy NA. Palivizumab for prophylaxis against respiratory syncytial virus infection in children with cystic fibrosis. *Cochrane Database Syst Rev*. 2012;(2):CD007743
 204. Winterstein AG, Eworuke E, Xu D, Schuler P. Palivizumab immunoprophylaxis effectiveness in children with cystic fibrosis. *Pediatr Pulmonol*. 2013;48(9):874–884
 205. Cohen AH, Boron ML, Dingivan C. A phase IV study of the safety of palivizumab for prophylaxis of RSV disease in children with cystic fibrosis [abstract]. *American Thoracic Society Abstracts*, 2005 International Conference; 2005. p. A178
 206. Giusti R. North American synagis prophylaxis survey. *Pediatr Pulmonol*. 2009;44(1):96–98
 207. El Saleeby CM, Somes GW, DeVincenzo HP, Gaur AH. Risk factors for severe respiratory syncytial virus disease in children with cancer: the importance of lymphopenia and young age. *Pediatrics*. 2008;121(2):235–243
 208. Berger A, Obwegeser E, Aberle SW, Langgartner M, Popow-Kraupp T. Nosocomial transmission of respiratory syncytial virus in neonatal intensive care and intermediate care units. *Pediatr Infect Dis J*. 2010;29(7):669–670
 209. Ohler KH, Pham JT. Comparison of the timing of initial prophylactic palivizumab dosing on hospitalization of neonates for respiratory syncytial virus. *Am J Health Syst Pharm*. 2013;70(15):1342–1346
 210. Blanken MO, Robers MM, Molenaar JM, et al. Respiratory syncytial virus and recurrent wheeze in healthy preterm infants. *N Engl J Med*. 2013;368(19):1794–1799
 211. Yoshihara S, Kusuda S, Mochizuki H, Okada K, Nishima S, Simões EAF, C-CREW Investigators. Effect of palivizumab prophylaxis on subsequent recurrent wheezing in preterm infants. *Pediatrics*. 2013;132(5):811–818
 212. Hall CB, Douglas RG Jr, Geiman JM. Possible transmission by fomites of respiratory syncytial virus. *J Infect Dis*. 1980;141(1):98–102
 213. Sattar SA, Springthorpe VS, Tetro J, Vashon R, Keswick B. Hygienic hand antiseptics: should they not have activity and label claims against viruses? *Am J Infect Control*. 2002;30(6):355–372
 214. Picheansathian W. A systematic review on the effectiveness of alcohol-based solutions for hand hygiene. *Int J Nurs Pract*. 2004;10(1):3–9
 215. Hall CB. The spread of influenza and other respiratory viruses: complexities and conjectures. *Clin Infect Dis*. 2007;45(3):353–359
 216. Boyce JM, Pittet D; Healthcare Infection Control Practices Advisory Committee; HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force; Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR Recomm Rep*. 2002;51(RR-16):1–45, quiz CE1–CE4
 217. World Health Organization. Guidelines on hand hygiene in health care. Geneva, Switzerland: World Health Organization; 2009. Available at: http://whqlibdoc.who.int/publications/2009/9789241597906_eng.pdf. Accessed July 15, 2014
 218. Karanfil LV, Conlon M, Lykens K, et al. Reducing the rate of nosocomially transmitted respiratory syncytial virus. [published correction appears in *Am J Infect Control*. 1999;27(3):303] *Am J Infect Control*. 1999;27(2):91–96
 219. Macartney KK, Gorelick MH, Manning ML, Hodinka RL, Bell LM. Nosocomial respiratory syncytial virus infections: the cost-effectiveness and cost-benefit of infection control. *Pediatrics*. 2000;106(3):520–526
 220. Strachan DP, Cook DG. Health effects of passive smoking. 1. Parental smoking and lower respiratory illness in infancy and early childhood. *Thorax*. 1997;52(10):905–914
 221. Jones LL, Hashim A, McKeever T, Cook DG, Britton J, Leonardi-Bee J. Parental and household smoking and the increased risk of bronchitis, bronchiolitis and other lower respiratory infections in infancy: systematic review and meta-analysis. *Respir Res*. 2011;12:5
 222. Bradley JP, Bacharier LB, Bonfiglio J, et al. Severity of respiratory syncytial virus bronchiolitis is affected by cigarette smoke exposure and atopy. *Pediatrics*. 2005;115(1). Available at: www.pediatrics.org/cgi/content/full/115/1/e7
 223. Al-Shawwa B, Al-Huniti N, Weinberger M, Abu-Hasan M. Clinical and therapeutic variables influencing hospitalisation for bronchiolitis in a community-based paediatric group practice. *Prim Care Respir J*. 2007;16(2):93–97
 224. Carroll KN, Gebretsadik T, Griffin MR, et al. Maternal asthma and maternal smoking are associated with increased risk of bronchiolitis during infancy. *Pediatrics*. 2007;119(6):1104–1112
 225. Semple MG, Taylor-Robinson DC, Lane S, Smyth RL. Household tobacco smoke and admission weight predict severe bronchiolitis in infants independent of deprivation: prospective cohort study. *PLoS ONE*. 2011;6(7):e22425
 226. Best D; Committee on Environmental Health; Committee on Native American Child Health; Committee on Adolescence. From the American Academy of Pediatrics: Technical report—Secondhand and prenatal tobacco smoke exposure. *Pediatrics*. 2009;124(5). Available at: www.pediatrics.org/cgi/content/full/124/5/e1017
 227. Wilson KM, Wesgate SC, Best D, Blumkin AK, Klein JD. Admission screening for secondhand tobacco smoke exposure. *Hosp Pediatr*. 2012;2(1):26–33
 228. Mahabee-Gittens M. Smoking in parents of children with asthma and bronchiolitis in a pediatric emergency department. *Pediatr Emerg Care*. 2002;18(1):4–7
 229. Dempsey DA, Meyers MJ, Oh SS, et al. Determination of tobacco smoke exposure by plasma cotinine levels in infants and children attending urban public hospital clinics. *Arch Pediatr Adolesc Med*. 2012;166(9):851–856
 230. Rosen LJ, Noach MB, Winickoff JP, Hovell MF. Parental smoking cessation to protect young children: a systematic review and meta-analysis. *Pediatrics*. 2012;129(1):141–152
 231. Matt GE, Quintana PJ, Destaillets H, et al. Thirdhand tobacco smoke: emerging evidence and arguments for a multidisciplinary research agenda. *Environ Health Perspect*. 2011;119(9):1218–1226
 232. Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics*. 2012;129(3). Available at: www.pediatrics.org/cgi/content/full/129/3/e827
 233. Ip S, Chung M, Raman G, et al. *Breast-feeding and Maternal and Infant Health Outcomes in Developed Countries*. Rockville,

- MD: Agency for Healthcare Research and Quality; 2007
234. Dornelles CT, Piva JP, Marostica PJ. Nutritional status, breastfeeding, and evolution of infants with acute viral bronchiolitis. *J Health Popul Nutr.* 2007;25(3):336–343
235. Oddy WH, Sly PD, de Klerk NH, et al. Breast feeding and respiratory morbidity in infancy: a birth cohort study. *Arch Dis Child.* 2003;88(3):224–228
236. Nishimura T, Suzue J, Kaji H. Breastfeeding reduces the severity of respiratory syncytial virus infection among young infants: a multi-center prospective study. *Pediatr Int.* 2009;51(6):812–816
237. Petruzella FD, Gorelick MH. Duration of illness in infants with bronchiolitis evaluated in the emergency department. *Pediatrics.* 2010;126(2):285–290
238. von Linstow ML, Eugen-Olsen J, Koch A, Winther TN, Westh H, Høgh B. Excretion patterns of human metapneumovirus and respiratory syncytial virus among young children. *Eur J Med Res.* 2006;11(8):329–335
239. Sacri AS, De Serres G, Quach C, Boulianne N, Valiquette L, Skowronski DM. Transmission of acute gastroenteritis and respiratory illness from children to parents. *Pediatr Infect Dis J.* 2014;33(6):583–588
240. Taylor JA, Kwan-Gett TS, McMahon EM Jr. Effectiveness of an educational intervention in modifying parental attitudes about antibiotic usage in children. *Pediatrics.* 2003;111(5 pt 1). Available at: www.pediatrics.org/cgi/content/full/111/5pt1/e548
241. Kuzujanakis M, Kleinman K, Rifas-Shiman S, Finkelstein JA. Correlates of parental antibiotic knowledge, demand, and reported use. *Ambul Pediatr.* 2003;3(4):203–210
242. Mangione-Smith R, McGlynn EA, Elliott MN, Krogstad P, Brook RH. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior. *Pediatrics.* 1999;103(4 pt 1):711–718

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”/ or exp health care costs/ or exp health expenditures/)
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)”

CINAHL

(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 exp 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

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

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)”

CINAHL

(MM "Bronchiolitis+") AND

((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

MedLine

(("bronchiolitis"[MeSH]) OR ("respiratory syncytial viruses"[MeSH])

NOT "bronchiolitis obliterans"[All Fields])

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 "Bronchiolitis+") AND

((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 anti-bacterial 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+")

The Cochrane Library

Bronchiolitis

1. AND (Breast Feeding OR breastfeeding)
2. AND tobacco
3. AND (hand hygiene OR handwashing OR hand decontamination)

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

Shawn L. Ralston, Allan S. Lieberthal, H. Cody Meissner, Brian K. Alverson, Jill E. Baley, Anne M. Gadomski, David W. Johnson, Michael J. Light, Nizar F. Maraqa, Eneida A. Mendonca, Kieran J. Phelan, Joseph J. Zorc, Danette Stanko-Lopp, Mark A. Brown, Ian Nathanson, Elizabeth Rosenblum, Stephen Sayles III and Sinsi Hernandez-Cancio

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