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Research Article

**EVALUATION OF RECENT UPDATES REGARDING  
BRONCHIOLITIS MANAGEMENT AND OUTCOMES**

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**Abstract:**

**Background:** Bronchiolitis is the most common viral acute lower respiratory tract infection origin among infants. The disease mostly is self-limited but sometimes the increased severity can cause some serious impact. Unfortunately, clinical trials have failed to establish any specific effective therapy.

**Objective:** A lot of literature have been done in order to provide better outcomes for patients presented with bronchiolitis, in our review we aim to discuss the recent literature that discussed bronchiolitis diagnosis and management.

**Method:** PubMed database were used for articles selection. All relevant articles related to our review were chosen to cover the following topics: Bronchiolitis, Management, Diagnosis and Outcomes. We excluded other articles, which are not related to our objectives. The data have been extracted according to specific form to be reviewed by the authors.

**Conclusion:** The initial signs and symptoms of the infection starts with mucosal inflammation and irritation of the upper respiratory tract like congestion, rhinorrhea, and sneezing. Wheezing is considered as a cardinal prerequisite for the diagnosis of bronchiolitis. The guidelines recommended the reduction of unnecessary care in diagnosis such as laboratory testing or imaging with exceptions for severe level of the condition. Supportive care is still the mainstay of an evidence-based approach to the disease. It includes suctioning, supplemental oxygen, and hydration. Most of the cases will not require any pharmacological therapy. Moreover, the use of complementary and alternative medicine as alternative or adjunctive therapy has shown only improvement regarding the symptoms. In patients with recurrent wheezing after bronchiolitis treatment, montelukast may reduce the frequency of post-bronchiolitic wheezing without causing significant side effects.

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**INTRODUCTION:**

Bronchiolitis is the most common acute lower respiratory tract infection (LRTI) of viral origin among infants [1]. It is a self-limiting lower airway disease of infants and young children. In the United States, the annual incidence is 11.4% in children below 1 year of age and 6% in those aged 1-2 years. Approximately, 23-31% cases of bronchiolitis are associated with fever [2,3]. In the United Kingdom, third of the infants will develop bronchiolitis in the first year of life and 3% of all infants require hospital admissions. In England alone, there were 30,451 secondary care admissions for bronchiolitis between 2011 and 2012 [4]. Sometimes, the increased severity of the condition can cause some serious impact although it is mostly self-limited. Unfortunately, clinical trials have failed to establish any specific therapy as effective, despite the high volume and significant economic impact of the disease. Therefore, in our review we aim to discuss the recent literature that discussed bronchiolitis diagnosis and management

**METHODOLOGY:****Sample**

We performed comprehensive search using biomedical databases; Medline, and PubMed, for studies concerned with Bronchiolitis management and diagnosis published in English language. Keywords used in our search through the databases were as {Bronchiolitis, Management, Diagnosis and Outcomes}. More relevant articles were recruited from references lists scanning of each included study.

**Analysis**

No software was used, the data were extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes). Double revision of each author outcomes was applied to ensure the validity and minimize the errors.

**DISCUSSION:**

Bronchiolitis is the most common acute LRTI of viral origin among infants [1]. It is usually caused by a viral infection of the bronchiole with a wide spectrum of illness severity. Although multiple viruses can cause bronchiolitis such as human metapneumovirus and human rhinovirus (RV) but the commonest cause is respiratory syncytial virus (RSV) [5]. It accounts in the United States alone for approximately 125,000 hospitalizations and 250 infant deaths every year. Global estimates by the World Health Organization indicate that RSV accounts overall for more than 60% of acute respiratory infections in children [6]. The incubation period ranges from 2 to 8 days. Transmission of RSV infection happens due to

inoculation of the nasopharyngeal or conjunctival mucosa with respiratory secretions from infected individuals. The virus stays viable for up to 6 hours on hard surfaces, for 90 minutes on rubber gloves and for 20 minutes on skin. These long periods of viability and survival highlights the need for hand washing and contact precautions as an essential and cost-effective practice to limit the spread of infection, especially in clinic settings. Two RSV subgroups, A and B, are simultaneously present in most outbreaks, with the RSV-A subgroup tending to cause more severe illness [7]. Although RSV clearly plays a major role in bronchiolitis, the advent of molecular diagnostic techniques has revealed a diverse group of pathogens associated with severe bronchiolitis that requires hospitalization. The major non-RSV infectious pathogen for children with severe bronchiolitis is RV. The prevalence of RV bronchiolitis ranges widely between 20–40% in emergency department (ED) and hospital settings. According to (Papadopoulos et al.) [8], RV is associated with more severity compared to RSV. It led the patients to the hospital considerably faster than RSV [7,8].

The clinical respiratory effects appear from the initial damage of epithelial cells in the terminal bronchi leading to edema, inflammation, excessive mucus production, and epithelial cell sloughing. The initial signs and symptoms of the infection starts with mucosal inflammation and irritation of the upper respiratory tract like congestion, rhinorrhea, and sneezing. In the next few days, the lower respiratory tract gets involved clinically manifested by cough and increased work of breathing with use of accessory respiratory muscles to overcome the increased resistance of obstructed airways. The main features of bronchiolitis are wheezing and/or crackles on auscultation and increased respiratory effort characterized by tachypnoea and/or chest wall retractions and/or nasal flaring. Wheezing is considered as a cardinal prerequisite for the diagnosis of bronchiolitis. After the clinicians should make the diagnosis of bronchiolitis on the basis of the history and physical examinations, they should evaluate the clinical severity of the disease in order to decide outpatient or inpatient care for the patient. The general condition of the affected infant should be also evaluated. The normal behavior may indicate mild disease while infant's irritability or lethargy indicate moderate or severe disease. If the general appearance is toxic, the infant should be carefully evaluated for other causes that could possibly explain the situation. Poor oral fluid intake, inability to eat due to breathlessness are indicators of moderate or severe disease and the affected infant should be referred to the hospital [4,9]. There are not universally used

validated clinical scores of disease severity. There are some suggested scores but several limitations for the usage of severity scores were found in everyday practice. Nevertheless, (Ravaglia et Poletti) [10] suggested in their paper several general thresholds for hospitalization such as poor feeding, severe retractions, oxygen saturation of 92% or less, and a respiratory rate of 60/min or more. The use of chest radiography for diagnosis and management of bronchiolitis has also varied widely and is not recommended routinely [11,12]. Risk factors for severe disease in bronchiolitis include age younger than 12 weeks and underlying medical conditions such as premature birth, cardiopulmonary disease, and immunodeficiency [12]. Laboratory testing is not recommended because it was associated with longer hospital stay and higher cost without any significant benefit. However, urinalysis can be suggested because urinary tract infection is the most common co-infection associated with bronchiolitis [13].

The disease mostly is self-limited as mentioned earlier but sometimes the increased severity can cause some serious impact. Unfortunately, clinical trials have failed to establish any specific therapy as effective, despite the high volume and significant economic impact of the disease. Therefore, supportive care is still the mainstay of an evidence-based approach to the disease. Furthermore, overuse of ineffective therapy remains common in bronchiolitis, with overuse of  $\beta$ -agonists, corticosteroids, antibiotics, viral testing, and chest radiography all well documented. Quality Improvement strategies in Hospitalization for Bronchiolitis by (Ralston et al.) [14] recommended the reduction of unnecessary care in children hospitalized for acute viral bronchiolitis.

Supportive treatment includes suctioning, supplemental oxygen, and hydration. Nasal suctioning provides relief of respiratory distress from the presence of copious secretions. In the 2013 Cochrane review, the length of stay (LOS) in hospital was shorter and the clinical severity scores were lower in those treated with hypertonic saline nebulization compared to normal saline [15]. Moreover, nebulized hypertonic saline reduced the risk of hospitalization by 14% compared with nebulized 0.9% saline among infants who were outpatients and those treated in the ED according to the 2017 Cochrane review [16,17]. In addition, (Heikkilä et al.) [18] evaluated the cost-effectiveness of hypertonic saline inhalations compared to normal saline inhalations or no inhalations and did not find any substantial cost-effectiveness either in the outpatient or inpatient settings. They suggested that the expected costs for treating infants with bronchiolitis are marginally lower for hypertonic

saline inhalations compared to control treatment. Although the costs were lower, the effectiveness of hypertonic saline inhalations was low as well, and even absent in the latest studies. However, (Heikkilä et al.) [18] concluded that the hypertonic saline inhalations were marginally cost-effective in the outpatient treatment of infant bronchiolitis but not in the inpatient treatment.

Supplemental oxygen may be initiated for patients with saturations  $<90\%$  while awake. The oxygen should be received warm and humidified. Hypoxemic Infants and refractory to supplemental oxygen, with persistent respiratory distress or developing respiratory failure require either noninvasive respiratory support with nasal continuous positive airway pressure (CPAP) or endotracheal intubation. (Pedersen et Vahlkvist) [19] conducted a study on 49 children with bronchiolitis experiencing signs of respiratory failure and required non-invasive respiratory support. They found that CPAP was superior to high flow nasal cannula (HFNC) in lowering respiratory rate and Fraction of inspired oxygen ( $FiO_2$ ) in infants with bronchiolitis. More than half of the children treated with HFNC were changed to CPAP treatment due to suspected treatment failure.

Due to congestion, fluid intake mostly decreases especially in infants. Therefore, fluid replacement therapy is highly required in these cases. Intravenous (IV) fluid hydration and nasogastric hydration are equally safe and effective methods to hydrate infants with bronchiolitis. Nasogastric hydration can be a better alternative for hydration and it was associated with a higher success rate of insertion. Nasogastric hydration was feasible and had comparable outcome with IV fluid hydration in any age without aspiration events or worsening of respiratory status [20,21,22].

Regarding pharmacologic therapy, there is no evidence supports the administration of systemic corticosteroids and/or inhaled  $\beta$ -agonist and/or epinephrine for the treatment of hospitalized patients with viral bronchiolitis, despite relentless attempts to identify pharmacologic strategies to improve the clinical course and outcomes of this Infection. However, inhaled  $\beta$ -agonists can be initiated single time in cases of personal or family history of atopy, asthma, or eczema. (Gadomski et Scribani) [23] meta-analysis which included 30 trials concluded that bronchodilators such as albuterol or salbutamol do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. Moreover, they were associated with adverse side effects such as tachycardia, tremors, and hypoxemia.

Similarly, evidence fails to show consistent benefit in the use of corticosteroids for infants and children with bronchiolitis. The role of corticosteroids in bronchiolitis presents a valid example of some of the present controversies. (Fernandes et al.) [24] conducted a review discussing the efficacy and safety of systemic and inhaled glucocorticoids and they summarized corticosteroids did not lead to a statistically significant reduction in outpatient admissions or hospital length of stay compared with placebo. The use of nebulized epinephrine for acute bronchiolitis is also not recommended.

Regarding antiviral medications, ribavirin is the only treatment approved by the US Food and Drug Administration for targeted treatment of RSV. Ribavirin is a synthetic nucleoside with broad antiviral activity that interferes with the RNA metabolism required for replication of viral genetic material. Typically, ribavirin is administered aerosolized for approximately 12 or more hours a day for 3 to 7 days. The effect of ribavirin is modest and cannot be reliable. Moreover, it is expensive. Therefore, it is suggested to be used only in immunocompromised patients or in patients with potentially life-threatening disease [6,12,25].

Although it is sometimes difficult to distinguish between viral and bacterial infections clinically and radiologically, antibiotics should not be overused in patients with viral bronchiolitis. Unfortunately, antibiotics overuse is often observed in clinical practice. However, children who progress to severe disease with respiratory failure and admitted to pediatric intensive care unit should receive empiric antibiotic therapy for bacterial co-infections [26].

The limited effectiveness of conventional medication has prompted the use of complementary and alternative medicine as alternative or adjunctive therapy for the management of bronchiolitis. (Kua et Lee) [27] reviewed 11 studies to determine the effectiveness and safety of complementary and alternative medicine for the treatment of bronchiolitis in infants aged less than 2 years. The evidence was not sufficient or rigorous enough to formulate recommendations for the use of any complementary and alternative medicine. Nevertheless, Chinese herbal medicine mixtures, vitamin D, N-acetylcysteine, and magnesium might be useful in managing the symptoms of bronchiolitis. Among studies that reported adverse events, no serious harms were noted.

Prevention is very important aspect during bronchiolitis infection. Multiple ways have been found to be highly effective in reducing the spread of RSV such as disinfection with alcohol-based rubs and hand washing with alcohol-based rubs or soap and

water. Also, the use of gloves and gowns can help in limiting transmission [6,12]. No vaccine exists today for active prophylaxis against RSV. Perhaps the most important success in the war against RSV so far has been the development of safe and effective passive prophylaxis. Palivizumab was licensed in June 1998 by the Food and Drug Administration for the reduction of serious LRTI caused by RSV in children at increased risk of severe disease. The drug showed significant reduction in the incidence of the disease. However, it is expensive and not widely available. Therefore, the guidelines do not recommend the use of Palivizumab except for patients at high risk for severe disease. High risk patients include preterm infants with chronic lung disease, infants with hemodynamically significant heart disease, children with pulmonary abnormality or neuromuscular disease that impairs the ability to clear secretions, and immunocompromised children younger than 24 months [28,29].

Many pediatric patients, especially those of very young age, continue to have recurrent episodes of lower airway obstruction after bronchiolitis treatment. (Peng et al.) [30] in their systematic review, assessed the efficacy of montelukast for preventing wheezing in patients with post-bronchiolitis. They found that montelukast may reduce the frequency of post-bronchiolitic wheezing without causing significant side effects but that it has no effects on decreasing incidences of recurrent wheezing, symptom-free days, or the associated usage of corticosteroid in post-bronchiolitis patients. Montelukast is an orally administered active compound. It binds with high affinity and selectivity to the Cysteinyl Leukotriene 1 (CysLT1) receptor and inhibits the physiologic actions of the anaphylaxis-related Leukotriene D4 (LTD4) at the CysLT1 receptor. CysLTs are suggested to be behind the pathogenesis of respiratory symptoms that develop due to viral-induced bronchiolitis [30,31].

(Norwood et al.) [32] tried to determine predictors of unscheduled visits after discharge from the ED. They found 3 independent predictors of post-ED unscheduled visits by children with bronchiolitis who are discharged following their initial ED visit. There 3 predictors are age younger than 2 months, male sex, and previous hospitalization. So, it is recommended to provide strict anticipatory guidance instructions and close primary care follow-up for those children with bronchiolitis at high risk of post-ED unscheduled visits.

#### CONCLUSION:

The initial signs and symptoms of the infection starts with mucosal inflammation and irritation of the upper

respiratory tract like congestion, rhinorrhea, and sneezing. Wheezing is considered as a cardinal prerequisite for the diagnosis of bronchiolitis. The guidelines recommended the reduction of unnecessary care in diagnosis such as laboratory testing or imaging with exceptions for severe level of the condition. Supportive care is still the mainstay of an evidence-based approach to the disease. It includes suctioning, supplemental oxygen, and hydration. Most of the cases will not require any pharmacological therapy. Moreover, the use of complementary and alternative medicine as alternative or adjunctive therapy has shown only improvement regarding the symptoms. In patients with recurrent wheezing after bronchiolitis treatment, montelukast may reduce the frequency of post-bronchiolitic wheezing without causing significant side effects.

#### REFERENCES:

1. Dawson-Caswell M, Muncie HL Jr., Respiratory syncytial virus infection in children. *Am Fam Physician*. 2011;83(2):141–6.
2. El-Radhi, A. S., W. Barry, and S. Patel. "Association of Fever and Severe Clinical Course in Bronchiolitis." *Archives of Disease in Childhood* 81, no. 3 (1999): 231-34. doi:10.1136/adc.81.3.231.
3. Ahmad, Syed amir, Quais Mujawar, Mohammed Al Othman, Hashim Bin Salleh, and Mahmoud Abdelhadi Alsarfandi. "Clinical Profile of Bronchiolitis in Infants Younger than 90 Days in Saudi Arabia." *Journal of Emergencies, Trauma, and Shock* 7, no. 1 (2014): 49. doi:10.4103/0974-2700.125641.
4. NICE National Institute for Health and Care Excellence. Bronchiolitis in children: diagnosis and management (NG9). Spring Gardens, London [updated June 1, 2015]. nice.org.uk/guidance/ng9.
5. Mansbach, Jonathan M., Alexander J. Mcadam, Sunday Clark, Paul D. Hain, Robert G. Flood, Uchechi Acholonu, and Carlos A. Camargo. "Prospective Multicenter Study of the Viral Etiology of Bronchiolitis in the Emergency Department." *Academic Emergency Medicine* 15, no. 2 (2008): 111-18. doi:10.1111/j.1553-2712.2007.00034.x.
6. Piedimonte, Giovanni, and Miriam K. Perez. "Respiratory Syncytial Virus Infection and Bronchiolitis." *Pediatrics in Review* 35, no. 12 (2014): 519-30. doi:10.1542/pir.35-12-519.
7. Hasegawa, Kohei, Jonathan M. Mansbach, and Carlos A. Camargo. "Infectious Pathogens and Bronchiolitis Outcomes." *Expert Review of Anti-infective Therapy* 12, no. 7 (2014): 817-28. doi:10.1586/14787210.2014.906901.
8. Papadopoulos, Nikolaos G., Maria Moustaki, Mariza Tsolia, Apostolos Bossios, Eleni Astra, Anargiroula Prezerakou, Dimitrios Gourgiotis, and Dimitrios Kafetzis. "Association of Rhinovirus Infection with Increased Disease Severity in Acute Bronchiolitis." *American Journal of Respiratory and Critical Care Medicine* 165, no. 9 (2002): 1285-289. doi:10.1164/rccm.200112-118bc.
9. Fretzayas, Andrew, and Maria Moustaki. "Etiology and Clinical Features of Viral Bronchiolitis in Infancy." *World Journal of Pediatrics* 13, no. 4 (2017): 293-99. doi:10.1007/s12519-017-0031-8.
10. Ravaglia, Claudia, and Venerino Poletti. "Recent Advances in the Management of Acute Bronchiolitis." *F1000Prime Reports* 6 (2014). doi:10.12703/p6-103.
11. Schuh, Suzanne, Amina Lalani, Upton Allen, David Manson, Paul Babyn, Derek Stephens, Shannon Macphee, Matthew Mokanski, Svetlana Khaikin, and Paul Dick. "Evaluation of the Utility of Radiography in Acute Bronchiolitis." *The Journal of Pediatrics* 150, no. 4 (2007): 429-33. doi:10.1016/j.jpeds.2007.01.005.
12. Ralston, SL, Lieberthal AS, Meissner HC, Et Al. "Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis." *Pediatrics*. 2014;134(5):e1474-e1502." *Pediatrics* 136, no. 4 (2015): 782. doi:10.1542/peds.2015-2862.
13. Librizzi, J., R. Mcculloh, K. Koehn, and B. Alverson. "Appropriateness of Testing for Serious Bacterial Infection in Children Hospitalized With Bronchiolitis." *Hospital Pediatrics* 4, no. 1 (2014): 33-38. doi:10.1542/hpeds.2013-0073.
14. Ralston, SL, A. Comick, E. Nichols, D. Parker, and P. Lanter. "Effectiveness of Quality Improvement in Hospitalization for Bronchiolitis: A Systematic Review." *Pediatrics* 134, no. 3 (2014): 571-81. doi:10.1542/peds.2014-1036.
15. Zhang, Linjie, Raúl A. Mendoza-Sassi, Claire Wainwright, and Terry P. Klassen. "Nebulised Hypertonic Saline Solution for Acute Bronchiolitis in Infants." *Cochrane Database of Systematic Reviews*, 2013. doi:10.1002/14651858.cd006458.pub3.
16. Zhang, Linjie, Raúl A. Mendoza-Sassi, Claire Wainwright, and Terry P. Klassen. "Nebulised Hypertonic Saline Solution for Acute Bronchiolitis in Infants." *Cochrane Database of Systematic Reviews*, 2017.

- doi:10.1002/14651858.cd006458.pub4.
17. Baron, Jeffrey, and Gladys El-Chaar. "Hypertonic Saline for the Treatment of Bronchiolitis in Infants and Young Children: A Critical Review of the Literature." *The Journal of Pediatric Pharmacology and Therapeutics* 21, no. 1 (2016): 7-26. doi:10.5863/1551-6776-21.1.7.
  18. Heikkilä, Paula, Minna Mecklin, and Matti Korppi. "The Cost-effectiveness of Hypertonic Saline Inhalations for Infant Bronchiolitis: A Decision Analysis." *World Journal of Pediatrics* 14, no. 1 (2018): 26-34. doi:10.1007/s12519-017-0112-8.
  19. Pedersen, Majken Bisgaard, and Signe Vahlkvist. "Comparison of CPAP and HFNC in Management of Bronchiolitis in Infants and Young Children." *Children* 4, no. 4 (2017): 28. doi:10.3390/children4040028.
  20. Oakley, Ed, Meredith Borland, Jocelyn Neutze, Jason Acworth, David Krieser, Stuart Dalziel, Andrew Davidson, Susan Donath, Kim Jachno, Mike South, Theane Theophilos, and Franz E. Babl. "Nasogastric Hydration versus Intravenous Hydration for Infants with Bronchiolitis: A Randomised Trial." *The Lancet Respiratory Medicine* 1, no. 2 (2013): 113-20. doi:10.1016/s2213-2600(12)70053-x.
  21. Oakley, Ed, Sonny Bata, Sharmila Rengasamy, David Krieser, John Cheek, Kim Jachno, and Franz E. Babl. "Nasogastric Hydration in Infants with Bronchiolitis Less Than 2 Months of Age." *The Journal of Pediatrics* 178 (2016). doi:10.1016/j.jpeds.2016.07.012.
  22. Kugelman, Amir, Karine Raibin, Husein Dabbah, Irina Chistyakov, Isaac Srugo, Lea Even, Nurit Bzezinsky, and Arieh Riskin. "Intravenous Fluids versus Gastric-Tube Feeding in Hospitalized Infants with Viral Bronchiolitis: A Randomized, Prospective Pilot Study." *The Journal of Pediatrics* 162, no. 3 (2013). doi:10.1016/j.jpeds.2012.10.057.
  23. Gadomski, Anne M., and Melissa B. Scribani. "Bronchodilators for Bronchiolitis." *Cochrane Database of Systematic Reviews*, 2014. doi:10.1002/14651858.cd001266.pub4.
  24. Fernandes, Ricardo M., Liza M. Bialy, Ben Vandermeer, Lisa Tjosvold, Amy C. Plint, Hema Patel, David W. Johnson, Terry P. Klassen, and Lisa Hartling. "Glucocorticoids for Acute Viral Bronchiolitis in Infants and Young Children." *Cochrane Database of Systematic Reviews*, 2013. doi:10.1002/14651858.cd004878.pub4.
  25. Ventre, Kathleen, and Adrienne Randolph. "Ribavirin for Respiratory Syncytial Virus Infection of the Lower Respiratory Tract in Infants and Young Children." *Cochrane Database of Systematic Reviews*, 2007. doi:10.1002/14651858.cd000181.pub3.
  26. Farley, Rebecca, Geoffrey Kp Spurling, Lars Eriksson, and Chris B Del Mar. "Antibiotics for Bronchiolitis in Children under Two Years of Age." *Cochrane Database of Systematic Reviews*, 2014. doi:10.1002/14651858.cd005189.pub4.
  27. Kua, Kok Pim, and Shaun Wen Huey Lee. "Complementary and Alternative Medicine for the Treatment of Bronchiolitis in Infants: A Systematic Review." *Plos One* 12, no. 2 (2017). doi:10.1371/journal.pone.0172289.
  28. Brady MT, Byington CL, Davies HD, Edwards KM, Jackson MA, Maldonado YA, Murray DL, Orenstein WA, Rathore MH, Sawyer MH, Schutze GE, Willoughby RE, Zaoutis TE, Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, Johnson DW, Light MJ, Maraqa NF, Mendonca EA, Phelan KJ, Zorc JJ, Stanko-Lopp D, Hernández-Cancio S. "Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection." *Pediatrics* 134, no. 2 (2014): 415-20. doi:10.1542/peds.2014-1665.
  29. Brady MT, Byington CL, Davies HD, Edwards KM, Jackson MA, Maldonado YA, Murray DL, Orenstein WA, Rathore MH, Sawyer MH, Schutze GE, Willoughby RE, Zaoutis TE, Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, Johnson DW, Light MJ, Maraqa NF, Mendonca EA, Phelan KJ, Zorc JJ, Stanko-Lopp D, Hernández-Cancio S. "Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection." *Pediatrics* 134, no. 2 (2014). doi:10.1542/peds.2014-1666.
  30. Peng, Wan-Sheng, Xin Chen, Xiao-Yun Yang, and En-Mei Liu. "Systematic Review of Montelukast Efficacy for Preventing Post-bronchiolitis Wheezing." *Pediatric Allergy and Immunology* 25, no. 2 (2013): 143-50. doi:10.1111/pai.12124.
  31. Montuschi, P., and M. L. Peters-Golden. "Leukotriene Modifiers for Asthma Treatment." *Clinical & Experimental Allergy* 40, no. 12 (2010): 1732-741. doi:10.1111/j.1365-2222.2010.03630.x.
  32. Norwood, Agatha, Jonathan M. Mansbach, Sunday Clark, Muhammad Waseem, and Carlos A. Camargo. "Prospective Multicenter Study of Bronchiolitis: Predictors of an Unscheduled Visit

After Discharge From the Emergency Department." *Academic Emergency Medicine* 17, no. 4 (2010): 376-82. doi:10.1111/j.1553-2712.2010.00699.x.