Management of acute asthma exacerbations

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Purpose of review
Herein, we review the current guidelines for the management of children with an acute asthma exacerbation. We focus on management in the emergency department, inpatient, and ICU settings.

Recent findings
The most recent statistics show that the prevalence of asthma during childhood has decreased in certain demographic subgroups and plateaued in other subgroups. However, acute asthma accounts for significant healthcare expenditures. Although there are few, if any, newer therapeutic agents available for management of acute asthma exacerbations, several reports leveraging quality improvement science have shown significant reductions in costs of care as well as improvements in outcome.

Summary
Asthma is one of the most common chronic conditions in children and the most common reason that children are admitted to the hospital. Nevertheless, the evidence to support specific agents in the management of acute asthma exacerbations is surprisingly limited. The management of acute exacerbations focuses on reversal of bronchospasm, correction of hypoxia, and prevention of relapse and recurrence. Second-tier and third-tier agents are infrequently used outside of the ICU setting. Reducing the variation in treatment is likely to lead to lower costs and better outcomes.

Keywords
acute asthma, ICU, inpatient, quality improvement, status asthmaticus

INTRODUCTION

Asthma is the most common chronic disease of childhood and one of the most common reasons that children are admitted to the hospital [1]. Although several epidemiologic studies reported an increase in the prevalence of childhood asthma in the waning years of the 20th century, recent statistics suggest that the prevalence is decreasing in a number of demographic groups. More importantly, disparities between racial subgroups appear to have plateaued [2]. Regardless, asthma affects more than 7 million children (9.6% of all children) in the United States of America alone, and more than half of these children will suffer from at least one acute exacerbation every year [3]. Asthma costs the US healthcare system over $56 billion per year, with acute exacerbations accounting for more than 50% of total expenditures [4]. Acute asthma exacerbations are largely preventable. Indeed, the United States of America has the highest rate of asthma-related hospitalizations and mortality among all of the highest income peer nations in the Organisation for Economic Co-operation and Development [5]. A number of studies [6▪▪,7▪▪,8▪,9▪] have documented significant variation in the care of these patients, which likely increases the cost of care and potentially worsens outcome. Given these sobering statistics, there is a clear opportunity for utilizing quality improvement science to reduce variation, minimize costs, and improve outcomes. Herein, we will focus on the management of acute asthma exacerbations and highlight some of these opportunities for the care of these children.

STEPWISE APPROACH TO THE MANAGEMENT OF ACUTE ASTHMA

Currently, the key priorities for managing children with an acute asthma exacerbation are to reverse airflow obstruction with short-acting beta agonists (SABAs), correct hypoxia with supplemental oxygen, minimize the risk of relapse with the use of systemic corticosteroids, and prevent future exacerbations with the use of controller medications, such

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KEY POINTS

- The evidence to support the management of acute asthma exacerbations in children is limited, and for this reason, there is significant variation in care in the emergency department, inpatient, and ICU settings.
- A stepwise approach to acute asthma exacerbations is warranted, with a principal focus on reversal of bronchospasm, correction of hypoxia, and prevention of relapse and recurrence.
- A quality improvement approach to management of acute asthma exacerbations will minimize variations in care, leading to lower costs of care and better outcomes.

as inhaled corticosteroids (ICS) [10]. A stepwise approach to management based upon an objective assessment of the severity of the exacerbation is preferred. SABAs act to rapidly reverse airflow obstruction through smooth muscle relaxation and resulting bronchodilation. Aerosolized albuterol administration in either a repetitive or continuous fashion (again, depending upon the severity of the presentation) is the preferred agent of choice. For example, in a study comparing albuterol with levalbuterol, there was some benefit in prevention of emergency department (ED) visits during acute asthma exacerbations, but there was no net benefit in prevention of hospitalization [11▪]. Inhaled anticholinergic medications such as ipratropium bromide are also frequently used in conjunction with albuterol in the ED setting to maximize bronchodilation. There is currently interest in the use of tiotropium for the management of moderate asthma exacerbations in children [12]; however, most studies have not found significant benefit to the use of anticholinergics in the acute management of asthma outside the ED setting and never as the sole agent.

Mild hypoxemia is common in children with an acute asthma exacerbation, primarily as a result of ventilation–perfusion mismatch and at times due to worsening of intrapulmonary shunt as a result of beta-agonist-mediated reversal of normal hypoxic pulmonary vasoconstriction. For example, the mean oxygen saturation of over 1000 children presenting to the ED with an acute asthma exacerbation was $95 \pm 4\%$, whereas the oxygen saturation in those children who were subsequently admitted to the hospital was $93 \pm 5\%$ [13]. Severe hypoxemia is uncommon and should prompt evaluation for pneumonia or pneumothorax. Supplemental oxygen titrated to maintain an oxygen saturation of 93–95% appears to balance the need for treating hypoxia and avoiding the aggravation of ventilation–perfusion mismatch [14].

Systemic corticosteroids are the other mainstay of acute management of asthma exacerbation. Steroids act through anti-inflammatory mechanisms that reduce airway edema. They can be administered in oral or intravenous forms and should be initiated promptly in exacerbations. Current guidelines recommend either prednisone/prednisolone or dexamethasone. A meta-analysis of 18 randomized, controlled trials failed to show any meaningful difference in outcomes [length of stay (LOS), adverse events, and effectiveness] between dexamethasone and prednisolone [15▪]. However, more recent studies have demonstrated that dexamethasone has comparable results with a shorter LOS [16] and is noninferior to prednisolone [17▪]. Although dexamethasone has a higher cost than prednisolone, less-frequent dosing leads to a simpler regimen for providers and families. Finally, molecular markers of inflammation may be a useful tool in the future for predicting steroid responsiveness of patients and has been shown to be more predictive than clinical phenotypes [18▪].

ICS are a mainstay of outpatient treatment for prevention of asthma exacerbations. However, some research has investigated the potential for increased dosing of ICS to prevent ED visits and hospital admissions and improve outcomes. A recent meta-analysis concluded that there was no improvement in admission rates with double-dose ICS, however [19▪]. Given recommendations to use ICS as controller therapy for persistent asthma, prescribing ICS at the time of discharge from the emergency care setting may be a cost-effective approach to minimizing the risk of recurrent asthma exacerbations [20].

ADJUNCTIVE TREATMENTS FOR ACUTE ASTHMA

Intravenous magnesium sulfate ($MgSO_4$) relieves bronchospasm by acting as a surrogate for calcium and causing smooth muscle relaxation. It mitigates both entry of extracellular calcium and release of calcium from intracellular stores, which decreases cytosolic calcium and thus smooth muscle cell contractility. A recent Cochrane review found that the use of IV $MgSO_4$ in the ED led to fewer hospitalizations, although the available studies were hindered by their small sample size [21▪,22]. Although the majority of reports involve the use of intermittent or one-time doses of $MgSO_4$, a recently published study [23▪] showed that continuous infusions of $MgSO_4$ in the ED led to shorter LOSs, higher proportion of discharges home at 24 h, and no adverse events. These findings are supported by pharmacologic data indicating that the pharmacokinetic effects of

magnesium are short-lived and that the effective doses may be higher than what are most commonly used in the ED setting [24▪]. More work is needed to determine optimum dosing and validate the initial findings of this study [25▪]. Of interest, several recent studies have investigated the effects of nebulized $MgSO_4$ in the ED setting. Nebulized $MgSO_4$ is particularly attractive given the theoretical absence of systemic side effects (primarily hypotension) and easier route of administration (which obviates the need for vascular access). In a recent randomized trial, the addition of nebulized magnesium to standard of care did not show any improvement in time to discharge. This finding was replicated in a meta-analysis of four available studies [26▪]. Despite these results, however, an additional randomized controlled trial of nonresponders to standard of care is currently being planned [27▪].

Terbutaline is a parenterally administered (most commonly) SABA that enhances ventilation by dilating constricted airways to reach lung segments that are not being adequately ventilated and thereby not 'seeing' inhaled beta agonist. Similar effects are observed with intramuscular epinephrine and intravenous salmeterol (not currently available in the United States of America). Terbutaline has a short half-life and must be administered by continuous infusion. Terbutaline has the potential to cause worsening tachycardia and hypotension, and therefore some clinicians may limit the use of this medication, especially in the adolescent age group in which tachycardia may not be as well tolerated. The safety of terbutaline was recently examined. In this study, all patients had sinus tachycardia after starting terbutaline therapy, but their heart rates improved to below baseline once terbutaline was discontinued. In addition, there was a decrease in both SBP and DBP. Of these, only a small percentage required inotropic support, and the vast majority of those patients were also receiving mechanical ventilatory support [28▪]. Nonetheless, given the potential for cardiac toxicity (primarily due to myocardial ischemia), several centers, including our own, monitor serial cardiac troponins and limit the use of terbutaline to the ICU setting.

Theophylline (or aminophylline) is a methylxanthine derivative that acts as a phosphodiesterase inhibitor to cause bronchodilation without affecting ventilation–perfusion matching. Historically, theophylline has fallen out of favor due to availability of better agents (i.e., albuterol) and the need to follow levels closely given its narrow therapeutic range and variable pharmacokinetics. However, a recent review published in the last year that included 10 randomized control trials showed that there is no difference in outcomes between children with 'ideal' therapeutic levels of 10–20 μg/ml compared with children with subtherapeutic levels less than 10 μg/ml [29▪]. In addition, there was no difference in the rate of adverse effects when comparing ideal levels with 'supratherapeutic' levels of more than 20 μg/ml. Another systematic review found a lack of evidence for dosing guidelines of aminophylline, and titrating based on levels did not improve safety or efficacy [30▪]. The lack of clinical difference between subtherapeutic and therapeutic levels of theophylline may be explained by theophylline's other mechanism of action. Theophylline may improve responsiveness to steroids by restoring histone deacetylase-2 activity. In a retrospective analysis, patients who received low-dose theophylline in addition to standard of care had significantly shorter LOS, time to discharge, time to space albuterol, and reduced costs [31▪]. Further studies of theophylline would appear to be warranted, particularly in those critically ill children who are refractory to first-tier agents, IV $MgSO_4$, and/or terbutaline.

Ketamine also has potent bronchodilatory effects in addition to the benefit of providing sedation to improve compliance in those patients requiring noninvasive positive pressure ventilation (NIPPV). It is also the induction agent of choice for tracheal intubation in critically ill children with acute respiratory failure secondary to status asthmaticus. There is little evidence to support the widespread use of ketamine. However, when ketamine was compared with aminophylline, both showed similar improvement in asthma scores, though there was no comparison with a placebo group [32▪]. A systematic review of ketamine in status asthmaticus concluded that it is a reasonable option in severe asthma management given its safety profile and potential benefits [33▪].

The additional benefit of ketamine lies in its sedative properties (mentioned above) to improve compliance of children requiring either noninvasive or invasive positive pressure ventilation. Early use of continuous positive airway pressure in asthmatics may be beneficial, even when initiated in the ED setting [34▪]. A recent Cochrane review that evaluated two randomized control trials compared patients receiving standard of care with those receiving NIPPV [35▪]. Given that these trials included less than 100 patients and had a high risk of bias, they were unable to confirm or reject the hypothesis that NIPPV was beneficial. Clearly, larger randomized trials are necessary.

NIPPV appears to improve the work of breathing associated with increased airway resistance and the consequent effects of dynamic hyperinflation (auto-PEEP). The higher intrathoracic pressures associated with dynamic hyperinflation create a scenario in

which the spontaneously breathing patient must generate a greater change in intrapleural pressure to generate airflow. Theoretically, NIPPV reduces the need for these drastic changes in intrapleural pressure, thereby relieving the work of breathing. The 'stenting' effect of NIPPV on the airways may also improve airway resistance. As such, NIPPV, if applied early (facilitated by the concomitant administration of ketamine), may prevent the need for tracheal intubation in children with severe bronchospasm and respiratory failure. Unfortunately, there are no specific recommendations for the timing of tracheal intubation in these patients. It is still generally accepted that patients in cardiac arrest, coma, and/or impending respiratory arrest should be tracheally intubated. The risks of intubation in asthmatic patients are well known and include cardiovascular collapse at the time of intubation, as well as barotrauma and ongoing difficulties with ventilation due to severe obstruction during the passive expiratory phase. Beyond these absolute indications, the decision on timing of tracheal intubation must be made on a case-by-case basis by the treating physician [1]. Inhaled anesthetics as adjunctive therapy for critically ill children with refractory status asthmaticus and acute respiratory failure have been described in a number of case reports. The most recent involved a case series of seven pediatric patients who required sevoflurane inhalation after exhausting all other conventional therapies. All seven patients in this study had significant improvement in pCO_2 and other clinical parameters [36]. There is no recent literature evaluating the use of Extracorporeal Membrane Oxygenation (ECMO) for asthma treatment in the pediatric population. In the adult population, a case report of 16 patients treated over 4 years with ECMO showed 100% survival without neurologic sequelae and had significant improvement in oxygenation, acidosis, and hypercarbia [37]. Obviously, inhaled anesthetics and/or ECMO likely require transfer to a tertiary or quarternary care facility with experience with these modalities.

ACUTE ASTHMA EXACERBATIONS: OPPORTUNITIES FOR IMPROVEMENT

A number of studies have documented significant variation in the management of children with acute asthma exacerbations in the ED setting. For example, children evaluated in nonpediatric EDs are more likely to receive blood tests (e.g., blood gas), radiography, and antibiotics than those seen in pediatric EDs [6▪▪]. In addition, even in pediatric EDs chest radiographs (presumably to rule out pneumonia) are likely overutilized [9▪]. There is also significant variation in the testing, treatment, and adherence to guidelines in the inpatient acute care [7▪▪] and intensive care settings [8▪], likely as a result of the lack of evidence for most of the therapies discussed above. Variation in care leads to excessive costs and potentially worse outcomes. Finally, and perhaps most importantly, there is a significant opportunity to reduce the incidence of hospital readmissions by improving processes around discharge (either from the ED or inpatient setting), especially by providing simple, easy-to-read materials that meet the needs of patients with a wide range of medical literacy [38].

There are a number of ongoing efforts focused on these and other issues with the goal of preventing acute asthma exacerbations, the need for hospitalization, and the incidence of hospital readmissions. In the ED, implementation of a standardized asthma protocol has been shown to improve adherence to NIH guidelines and improved timeliness of administration of beta-agonists, ipratropium, and corticosteroids [39▪]. This could potentially lead to shorter LOS in the ED and fewer admissions [40▪]. In addition, standardizing admission criteria can also lead to reduced LOS in the ED for admitted patients [41▪]. Even after the initial implementation, fine-tuning and reevaluating these pathways can lead to sustained improvement [42▪].

Several quality initiatives have also focused on improving care after admission to the hospital. For example, by implementing order sets and asthma clinical pathways, one study showed a reduction in costs, decreased LOS, and decreased use of respiratory treatments [43▪]. Even by simply implementing a discharge criterion, LOS for asthmatics improved by an average of 8 h, with no change in readmission rate [44]. On a larger scale, a tertiary hospital and its surrounding community hospitals all implemented one clinical practice guideline to standardize care and improve compliance with previously published quality measures. After implementation, there was a sustained improvement in compliance with guidelines, reduced LOS, and reduced readmission rates [45▪▪]. Across the United States of America, improved adherence to evidence-based guidelines has decreased hospital LOS [7▪▪].

At the time of discharge, the odds of returning to the ED within the next 30 days can be lowered simply by discharging patients with medications already in hand (vs. handing patients a prescription) [46▪]. Creating partnerships between hospitals and local pharmacies to facilitate this 'meds-in-hand' initiative is an effective intervention to reduce reutilization of emergency and inpatient services [47▪]. This effect is even seen in the ED setting, in which discharging patients with albuterol in hand led to reduced reutilization [48▪]. In addition, the way

nurses are instructed to discharge patients can reduce exposure to asthma triggers at home by up to 60% [49]. A recent retrospective analysis of nearly 10 000 patients hospitalized with asthma showed that a higher rate of readmission occurred in patients who had a preceding hospitalization or ED visit within the previous 6 months or had a prescription for corticosteroids filled in between initial hospitalization discharge and readmission [50▪]. These clinical parameters may help identify patients with more severe asthma that may require improved education or increased controller medications.

CONCLUSION

Although recent statistics suggest a decreasing pediatric asthma prevalence, acute asthma exacerbations continue to account for significant healthcare expenditures. Improved adherence to clinical guidelines may improve outcomes on a wider scale. In addition, in those patients with acute asthma exacerbations that are refractory to the currently recommended treatments (supplemental oxygen, SABA, and corticosteroids), the use of second-tier and third-tier therapies may be beneficial. Finally, a quality improvement approach to the management of these patients along the continuum of care may have the greatest impact on outcomes and the costs of care.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Pardue Jones B, Fleming GM, Otillio JK, Asokan I. Pediatric acute asthma exacerbations: evaluation and management from emergency department to intensive care unit. J Asthma 2016; 53:607.
2. Akinbami LJ, Simon AE, Rossen LM. Changing trends in asthma prevalence among children. Pediatrics 2016; 137:e20152354.
3. Akinbami OJ, Moorman JE, Liu X, *et al.* Asthma prevalence, healthcare use, and mortality: United States, 2005–2009. Washington, DC: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2011. https://www.aap.org/en-us/Documents/medicalhome_resources_asthma_prevalence.pdf. [Accessed 7 January 2017]
4. Barnett SBL, Nurmagambetov TA. Costs of asthma in the United States: 2002–2007. J Allergy Clin Immunol 2011; 127:145–152.
5. Woolf S, Aron L. Health in international perspective: shorter lives, poorer health. National Research Council (US), Institute of Medicine (US), editors. Washington (DC): National Academies Press (US); 2013.
6. ▪▪ Chamberlain JM, Teach SJ, Hayes KL, *et al.* Practice pattern variation in the care of children with acute asthma. Acad Emerg Med 2016; 23:166–170.
This cross-sectional analysis based on data from the National Hospital Ambulatory Medical Care Survey reviewed use of CBCs, CXRs, and antibiotics in the treatment of acute asthma exacerbation. Though recent guidelines have recommended low rates of use for these tests/treatments, this study found high rates of variability across the nation and found lower rates of utilization in pediatric-specific emergency departments (EDs), indicating a potential source of overuse in nonpediatric EDs.
7. ▪▪ Hasegawa K, Tsugawa Y, Clark S, *et al.* Improving quality of acute asthma care in US hospitals. Chest 2016; 150:112–122.
This multicenter retrospective study evaluated guideline concordance for asthma care and found that overall guideline concordance improved from 2000 to 2013 for adults and pediatric asthma care; however, wide variability remains in asthma care. Those hospitals with better guideline concordance had reduced length of stay (LOS) for asthma exacerbations.
8. ▪ Dilley MA, Sheehan WJ, Petty CR, *et al.* Comparison of treatment modalities for inpatient asthma exacerbations among US pediatric hospitals. J Allergy Clin Immunol Pract 2016. [Epub ahead of print]
This article demonstrated significant variation in pediatric ICU utilization of several treatment regimens.
9. ▪ Florin TA, Carron H, Huang G, *et al.* Pneumonia in children presenting to the emergency department with an asthma exacerbation. JAMA Pediatr 2016; 170:803–805; http://archpedi.jamanetwork.com/article.aspx?articleID=2527082. [Accessed 23 December 2016]
This study used data from the pediatric health information system to compare use of radiography in acute asthma exacerbations. There were significant differences in rates of testing across member institutions, with higher testing hospitals having higher rates of inpatient admission.
10. National Asthma Education and Prevention Program. Third expert panel on the diagnosis and management of asthma. In: Expert panel report 3: guidelines for the diagnosis and management of asthma. Bethesda, MD: National Heart, Lung, and Blood Institute; 2007.
11. ▪ Yuan J, Lu ZK, Zhang Y, *et al.* Clinical outcomes of levalbuterol versus racemic albuterol in pediatric patients with asthma: propensity score matching approach in a medicaid population: clinical outcomes of levalbuterol versus albuterol. Pediatr Pulmonol 2016. [Epub ahead of print]
This retrospective cohort study using the medicaid database for South Carolina to compare the effect of levalbuterol and albuterol use on subsequent asthma exacerbation utilization, accounting for differences in baseline cohorts using propensity score matching. In this study, levalbuterol use was associated with decreased ED utilization, but not decreased hospital admission.
12. Vogelberg C. Emerging role of long-acting anticholinergics in children with asthma. Curr Opin Pulm Med 2016; 22:74–79.
13. Keahey L, Bulloch B, Becker AB, *et al.* Initial oxygen saturation as a predictor of admission in children presenting to the emergency department with acute asthma. Ann Emerg Med 2002; 40:300–307.
14. Perrin K, Wijesinghe M, Healy B, *et al.* Randomised controlled trial of high concentration versus titrated oxygen therapy in severe exacerbations of asthma. Thorax 2011; 66:937–941.
15. ▪ Normansell R, Kew KM, Mansour G. Different oral corticosteroid regimens for acute asthma. In: The Cochrane Collaboration, editor. Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016 ; http://doi.wiley. com/10.1002/14651858.CD011801.pub2. [Accessed 23 December 2016]
This is a Cochrane Review that evaluated 18 studies comparing oral steroid regimens to evaluate effectiveness of different types and doses of steroid medications. Overall, there was no convincing evidence of superiority of longer courses vs. shorter courses or of dexamethasone vs. prednisolone.
16. Parikh K, Hall M, Mittal V, *et al.* Comparative effectiveness of dexamethasone versus prednisone in children hospitalized with asthma. J Pediatr 2015; 167:639–644.e1.
17. ▪ Cronin JJ, McCoy S, Kennedy U, *et al.* A randomized trial of single-dose oral dexamethasone versus multidose prednisolone for acute exacerbations of asthma in children who attend the emergency department. Ann Emerg Med 2016; 67:593–601.
This was a noninferiority study of single-dose dexamethasone vs. three doses of prednisolone for patients presenting to the ED with asthma exacerbation. It demonstrated no difference in symptoms or reutilization between the two groups.
18. ▪ Fitzpatrick AM, Stephenson ST, Brown MR, *et al.* Systemic corticosteroid responses in children with severe asthma: phenotypic and endotypic features. J Allergy Clin Immunol Pract 2016. [Epub ahead of print]
This study assessed response to steroids for children with severe asthma and demonstrated molecular markers that better predicted response to systemic steroid regimens.
19. ▪ Kew KM, Quinn M, Quon BS, Ducharme FM. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. In: The Cochrane Collaboration, editor. Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016; http://doi.wiley.com/10.1002/14651858.CD007524.pub4. [Accessed 23 December 2016]
This Cochrane review evaluated eight trials on the use of increased dosing of inhaled corticosteroids at home to prevent systemic steroid use or other adverse events.

20. Andrews AL, Russell WS, Titus MO, *et al.* Quality improvement methods improve inhaled corticosteroid prescribing in the emergency department. J Asthma 2014; 51:737–742.

21. Griffiths B, Kew KM. Intravenous magnesium sulfate for treating children with ■ acute asthma in the emergency department. In: The Cochrane Collaboration, editor. Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016. ; http://doi.wiley.com/10.1002/14651858.CD011050.pub2. [Accessed 23 December 2016]

This is a Cochrane review that evaluated the use of IV magnesium in the emergency department. They found that the use of IV magnesium led to fewer hospitalizations, although the available studies were hindered by small sample size.

22. Griffiths B, Kew KM, Normansell R. Intravenous magnesium sulfate for treating children with acute asthma in the emergency department. Paediatr Respir Rev 2016; 20:45–47.

23. Irazuzta JE, Paredes F, Pavlicich V, Domínguez SL. High-dose magnesium ■ sulfate infusion for severe asthma in the emergency department: efficacy study. Pediatr Crit Care Med 2016; 17:e29–e33.

This study was the first to evaluate high-dose infusion vs. small bolus dosing of IV magnesium. They found improved proportion of discharges home and shorter overall LOS in patients who were treated with high-dose infusion of IV magnesium.

24. Rower JE, Liu X, Yu T, *et al.* Clinical pharmacokinetics of magnesium sulfate in ■ the treatment of children with severe acute asthma. Eur J Clin Pharmacol 2017; 73:325–331.

This article evaluated pharmacokinetic of magnesium and concluded that the effective dose of magnesium is likely higher that what is typically used.

25. Liu X, Yu T, Rower JE, *et al.* Optimizing the use of intravenous magnesium ■ sulfate for acute asthma treatment in children: intravenous $MgSO_4$ for pediatric asthma. Pediatr Pulmonol 2016; 51:1414–1421.

This article was a review of the available literature regarding IV magnesium. They concluded that pharmacokinetic and pharmacodynamics are needed to be further evaluated for magnesium in children.

26. Su Z, Li R, Gai Z. Intravenous and nebulized magnesium sulfate for treating ■ acute asthma in children: a systematic review and meta-analysis. Pediatr Emerg Care 2016; 1. [Epub ahead of print]

This is a meta-analysis of the use of nebulized magnesium in treatment of asthma and did not find any improvement in time to discharge.

27. Schuh S, Sweeney J, Freedman SB, *et al.,* Pediatric Emergency Research ■ Canada Group. Magnesium nebulization utilization in management of pediatric asthma (MagNUM PA) trial: study protocol for a randomized controlled trial. Trials 2016; 17:261.

This article outlines the plan for randomized controlled trial of nebulized magnesium in addition to standard of care.

28. Doymaz S, Schneider J. Safety of terbutaline for treatment of acute severe ■ pediatric asthma. Pediatr Emerg Care 2016; 1. [Epub ahead of print]

This article evaluated the safety profile of terbutaline. Even though all patients had sinus tachycardia and lower blood pressures after initiating terbutaline, only a small percentage needed intervention.

29. Cooney L, Hawcutt D, Sinha I. The evidence for intravenous theophylline ■ levels between 10–20 mg/L in children suffering an acute exacerbation of asthma: a systematic review. PLoS One 2016; 11:e0153877.

This is a systematic review for the evidence of dosing guidelines for theophylline therapy. The absence of side effects with supratherapeutic levels as well as the finding of similar improvement with subtherapeutic levels calls into question the main hesitancy for using theophylline.

30. Cooney L, Sinha I, Hawcutt D. Aminophylline dosage in asthma exacerbations ■ in children: a systematic review. PLoS One 2016; 11:e0159965.

This systematic review found a lack of evidence for titrating aminophylline based on levels as this did not improve efficacy or safety.

31. Eid N, O'Hagan A, Bickel S, *et al.* Anti-inflammatory dosing of theophylline in ■ the treatment of status asthmaticus in children. J Asthma Allergy 2016; 9:183–189.

This retrospective analysis found that low-dose theophylline led to improved LOS and reduced costs.

32. Tiwari A, Guglani V, Jat KR. Ketamine versus aminophylline for acute asthma in ■ children: a randomized, controlled trial. Ann Thorac Med 2016; 11:283.

This article showed that there was similar improvements in asthma scores in patients when comparing aminophylline and ketamine, although there was no placebo group included.

33. Hendaus M, Jomha F, Alhammadi A. Is ketamine a lifesaving agent in ■ childhood acute severe asthma? Ther Clin Risk Manag 2016; 12:273–279.

This review of recent studies concluded that as ketamine has potential benefits and is relatively well tolerated, it is a reasonable option in severe asthma exacerbations.

34. Schibler A, Franklin D. Respiratory support for children in the emergency ■ department: respiratory support for children. J Paediatr Child Health 2016; 52:192–196.

This review article outlines the sequential steps for pediatric patients with respiratory distress in the ED. Early use of noninvasive positive pressure ventilation for asthmatic patients is potentially beneficial.

35. Korang SK, Feinberg J, Wetterslev J, Jakobsen JC. Noninvasive positive ■ pressure ventilation for acute asthma in children. In: The Cochrane Collaboration, editor. Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016. ; http://doi.wiley.com/10.1002/14651858.CD012067.pub2. [Accessed 23 December 2016]

This Cochrane review evaluated the use of noninvasive positive pressure ventilation (NIPPV) in acute asthma. There were only two studies included, so the authors were unable to determine if NIPPV was beneficial. Larger trials are needed.

36. Schutte D, Zwitserloot AM, Houmes R, *et al.* Sevoflurane therapy for life-threatening asthma in children. Br J Anaesth 2013; 111:967–970.

37. Di Lascio G, Prifti E, Messai E, *et al.* Extracorporeal membrane oxygenation support for life-threatening acute severe status asthmaticus. Perfusion 2017; 32:157–163.

38. Samuels-Kalow M, Rhodes K, Uspal J, *et al.* Unmet needs at the time of emergency department discharge. Acad Emerg Med 2016; 23:279–287.

39. Miller AG, Breslin ME, Pineda LC, Fox JW. An asthma protocol improved ■ adherence to evidence-based guidelines for pediatric subjects with status asthmaticus in the emergency department. Respir Care 2015; 60:1759–1764.

This article showed that by development and implementation of an asthma protocol there was improved adherence to evidence-based treatment guidelines.

40. Gray MP, Keeney GE, Grahl MJ, *et al.* Improving guideline-based care of ■ acute asthma in a pediatric emergency department. Pediatrics 2016; 138:e20153339–e20153339.

This quality improvement study achieved decreased time to first inhaled short-acting beta agonist treatment, decreased ED LOS, and decreased hospitalization in their institution.

41. Rutman L, Migita R, Spencer S, *et al.* Standardized asthma admission criteria ■ reduce length of stay in a pediatric emergency department. Acad Emerg Med 2016; 23:289–296.

This retrospective study of a quality improvement intervention on asthma in the ED demonstrated decreased ED LOS and time to bed request.

42. Rutman L, Atkins RC, Migita R, *et al.* Modification of an established pediatric ■ asthma pathway improves evidence-based, efficient care. Pediatrics 2016; 138:e20161248–e20161248.

This retrospective analysis of a revision to the ED asthma pathway revealed an improvement in adherence to care guidelines and decreased ED LOS.

43. Dayal A, Alvarez F. The effect of implementation of standardized, evidence-■ based order sets on efficiency and quality measures for pediatric respiratory illnesses in a community hospital. Hosp Pediatr 2015; 5:624–629.

This study evaluated the effect of asthma ordersets and an asthma pathway and demonstrated decreased LOS, decreased medication use, and decreased cost in patient care.

44. Chong C, Samson J, Lucia AD, *et al.* Criteria led discharge reduces length of hospital stay for children with acute asthma. J Asthma 2016; 53:1–1.

45. Nkoy F, Fassl B, Stone B, *et al.* Improving pediatric asthma care and outcomes ■■ across multiple hospitals. Pediatrics 2015; 136:e1602–e1610.

This article outlines a sustained effort to standardize care in a tertiary hospital and its surrounding community facilities. This standardized care was attained through the initiation of asthma protocols and led to decreased LOS as well as reduced readmission rates.

46. Hatoun J, Bair-Merritt M, Cabral H, Moses J. Increasing medication posses-■ sion at discharge for patients with asthma: the meds-in-hand project. Pediatrics 2016; 137:e20150461–e20150461.

This article highlighted the steps undertaken to improve medication possession at discharge. By ensuring that patients had discharge medications prior to leaving the hospital, the QI team was able to lower the rate of representing to the ED within 30 days.

47. Sauers-Ford HS, Moore JL, Guiot AB, *et al.* Local pharmacy partnership to ■ prevent pediatric asthma reutilization in a satellite hospital. Pediatrics 2016; 137:e20150039–e20150039.

This quality improvement study detailed a partnership with a community pharmacy in delivering medications prior to discharge for patients admitted for asthma exacerbation that led to reduced readmissions for patients.

48. Hall AB, Novotny A, Bhisitkul DM, *et al.* Association of emergency department ■ albuterol dispensing with pediatric asthma revisits and readmissions. J Asthma 2016; 1–6. [Epub ahead of print]

This retrospective cohort study evaluated the effect of direct dispensing of albuterol inhalers to patients discharged home from the ED. It demonstrated a decrease in ED reutilization for patients receiving albuterol inhalers for home use prior to discharge.

49. Ekim A, Ocakci AF. Efficacy of a transition theory-based discharge planning program for childhood asthma management. Int J Nurs Knowl 2016; 27:70–78; http://onlinelibrary.wiley.com/doi/10.1111/2047-3095.12077/pdf. [Accessed 23 December 2016]

50. Brittan M, Richardson T, Kenyon C, *et al.* Association between postdischarge ■ oral corticosteroid prescription fills and readmission in children with asthma. J Pediatr 2017; 180:163–169.e1.

This was a retrospective analysis that aimed to evaluate risk factors for readmission. Those patients who had an ED visit of hospitalization in the preceding 6 months or oral corticosteroid use after initial discharge were at higher rates of readmission.