10-2016

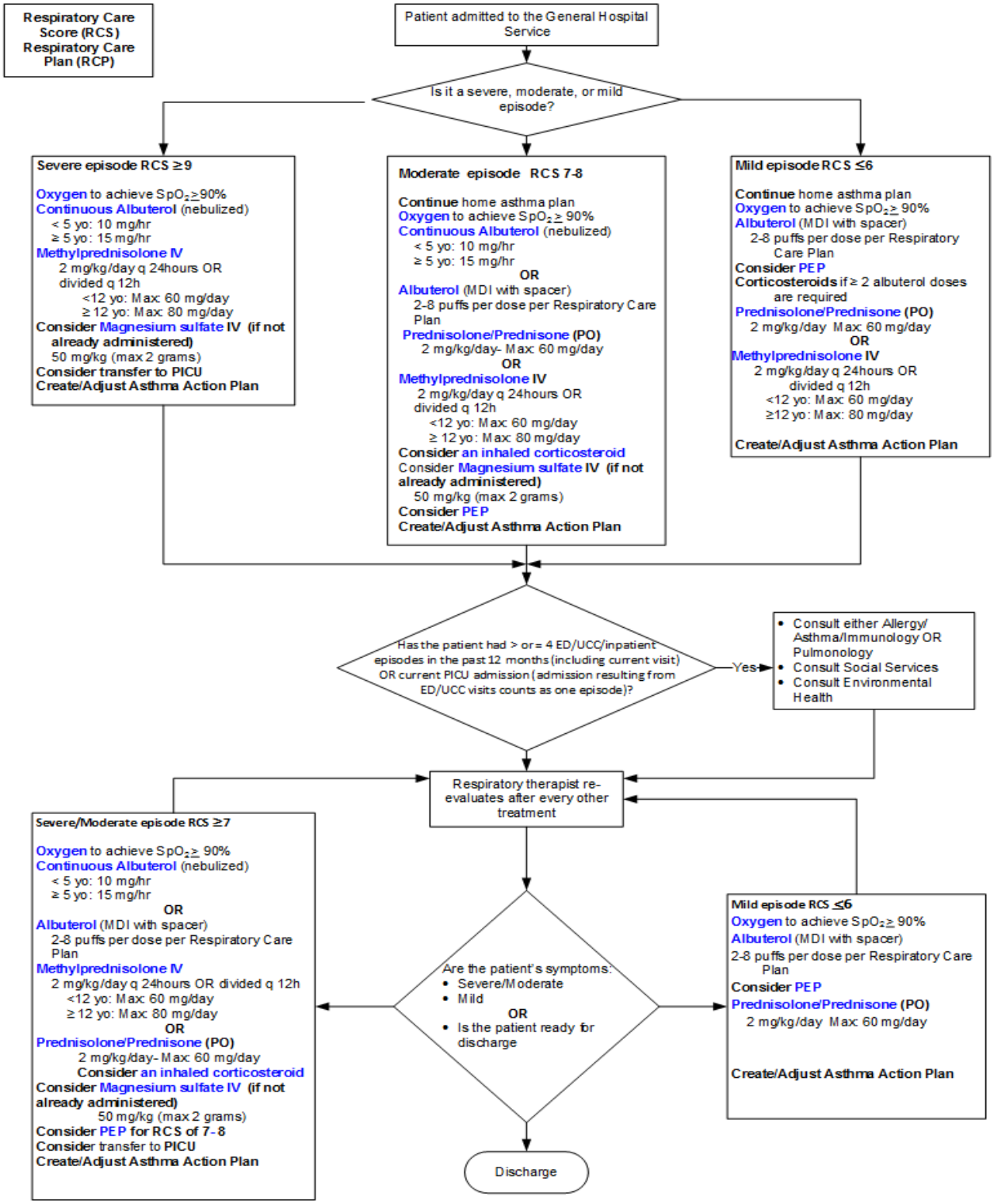
Asthma—Inpatient

Children's Mercy Kansas City

October 2016

Children's Mercy Hospital, Kansas City
Evidence Based Practice Clinical Practice Guide

Asthma—Inpatient



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Definition: Asthma is a chronic inflammatory disorder of the airways characterized by recurrent and reversible airflow obstruction. Airways swell, and produce extra mucous in addition to bronchospasm, resulting in overall narrowing of the airway. Increased coughing, wheezing, and shortness of breath are typical symptoms. In the United States, more than 6 million children are affected with asthma (CDC, 2014) and in 2010, there were 439,000 hospital discharges with asthma listed as the first diagnosis (Bloom, Cohen, & Freeman, 2012).

Objective of Guideline: The objective of this guideline is to standardize the care of children seen on the inpatient units for asthma.

Target Users: Providers, staff nurses, and respiratory therapists caring for children with asthma on the inpatient units.

Guideline Inclusion Criteria: Children greater than or equal to 2 years of age and less than 18 years of age with symptoms consistent with asthma exacerbation, including difficulty breathing, coughing, and wheezing.

Guideline Exclusion Criteria:

- Children greater than 2 years of age admitted with first-time wheezing secondary to a known infection. Children with the following underlying conditions:
  - Severe gastroesophageal reflux
  - Cystic fibrosis
  - HIV with possible Pneumocystis pneumonia (PJP)
  - Immunodeficiency
  - History of chronic aspiration
  - Bronchopulmonary dysplasia
  - Tracheomalacia
  - History of lower airway surgery
  - Congenital heart disease

Differential Diagnosis: (in alphabetical order)

- Aspiration
- Bacterial pneumonia
- Bronchiolitis
- Croup
- Congestive heart disease
- Foreign body
- Inhalation injury

Clinical Questions Posed by the Guideline:

1. What level of oxygen saturation was used as a cutoff for initiation of supplemental oxygen for subjects in studies of asthma exacerbations?
2. What are the maximum doses of continuous albuterol?
3. In the child hospitalized with an asthma exacerbation, should intravenous fluids be routinely administered?
4. In the child hospitalized with an asthma exacerbation, should intravenous magnesium sulfate be used to improve pulmonary function?
5. In the child hospitalized with an asthma exacerbation, should more than one treatment with intravenous magnesium be given?

6. In the child hospitalized with an asthma exacerbation, should albuterol be administered by nebulizer or metered-dose inhaler (MDI) and spacer to improve pulmonary function?
7. In the child hospitalized with an asthma exacerbation, should methylprednisolone/prednisolone/prednisone vs. dexamethasone be used to improve pulmonary function?
8. In the child hospitalized with an asthma exacerbation, should inhaled steroids be initiated during an asthma exacerbation to improve pulmonary function or should inhaled corticosteroids be continued if the treatment is included on the child's home Asthma Action Plan?
9. In the child hospitalized with an asthma exacerbation, should positive expiratory pressure (PEP) therapy be used?
10. For the child who has had > or = to four ED/UCC/inpatient episodes in the last 12 months (including the current visit), what is the efficacy of consulting:
    - Allergy, Asthma, Immunology OR Pulmonary Medicine?
    - Social Services?
    - Environmental Health?

Practice Recommendations (EPR-3, 2007):
Inpatient asthma care is either:
The initiation of care for an exacerbation or the continuation of care received in the emergency department (ED) or other medical care setting. The following treatments are recommended for inpatients with asthma exacerbations:

1. Supplemental oxygen should be administered to maintain a SpO2 greater to or equal to 90-92%, unless otherwise directed.
2. Bronchodilators (for all patients) should be given.
3. Continue home controller medication, or consider starting an inhaled corticosteroid. We do not recommend treating an asthma exacerbation with inhaled corticosteroids ONLY.
4. Systemic corticosteroids (for most patients) should be given.

The dose and frequency of the three principal treatments (supplemental oxygen, albuterol, and systemic corticosteroids) are determined by the severity of the exacerbation.

The following adjunctive therapies may be helpful:

1. Intravenous magnesium
2. Positive Expiratory Pressure (PEP)

The administration of the following treatments is NOT recommended (in alphabetical order):

3. Aggressive hydration
4. Antibiotics (except as needed for concurrent infections or other conditions)
5. Chest physiotherapy
6. Methylxanthines
7. Mucolytics
8. Sedation

Physical Exam: Obtain vital signs, including SpO2. The physical exam of the respiratory system should include assessment of aeration throughout the lung fields, auscultation for wheezing, and the observation for the presence of increased work of breathing (accessory muscle use and retractions). Neurologic signs such as altered mental status, agitation, or drowsiness should be included in the exam. Cardiovascular

signs such as significant tachycardia and hypotension should be monitored closely, especially if continuous albuterol or magnesium was or will be given.

Diagnostics: Diagnostic testing, in general, is typically not necessary and should only be performed based on the clinical presentation of each patient. When diagnostic studies are deemed necessary, performing these tests should not hinder the treatment of the asthma exacerbation; they should occur simultaneously so as not to delay treatment. Chest x-rays do not have to be routinely obtained on all patients with asthma exacerbations. Peak flow and spirometry can provide useful information about the severity of obstruction a patient has; however, not all patients are able to adequately perform this testing in the midst of an acute exacerbation. An ABG can be obtained if there is concern that a patient is not adequately ventilating or oxygenating and is progressing toward respiratory failure. Usually, though, ABGs are not needed in the initial evaluation of a patient with an asthma exacerbation (EPR-3, 2007).

Respiratory Care Score (RCS): Utilizing information from the patient's history and physical exam, an RCS can be calculated. Multiple RCSs have been developed and studied in order to determine the severity of a patient's asthma exacerbation, predict hospital admission, and response to therapy. Various un-validated scoring systems have been developed and utilized by individual facilities to monitor response and to help guide therapy. Children's Mercy developed a tool that incorporates patient history and physical exam findings into a score, the RCS, which is incorporated into an overall Respiratory Care Plan (RCP).

Treatment:

- Continue or initiate supplemental oxygen to maintain a SpO2 ≥ 90-92%.
- Continue or initiate beta agonists (Mild/Moderate Asthma via MDI or Moderate/Severe Asthma via continuous nebulizer).
- Initiate or continue treatment with a systemic corticosteroid.
- Consider continuation of inhaled corticosteroids (if the patient uses inhaled corticosteroids at home) or initiation of inhaled corticosteroids.
- Consider treatment with intravenous magnesium sulfate, if the patient has not received this treatment.
- Consider PEP therapy, per the Respiratory Care Plan.

Discharge:

Prior to discharge the following tasks should be completed:

- Develop or adjust an Asthma Action Plan (AAP) for each patient.
- Provide education to each patient and parent(s)/guardian(s) about asthma, the medications used to treat asthma, the patient's AAP, and risk factors to avoid.
- Provide environmental health information and/or an environmental health assessment if a patient's history suggests that the patient's living environment significantly contributes to his/her asthma symptoms.
- Arrange for follow-up with the patient's Primary Care Provider (PCP) and/or with an Asthma Specialist.
- During the influenza season, offer the influenza vaccine prior to discharge if the patient has not received the annual influenza vaccine and has no specific contraindications to receiving it.

Measures:

Outcome measures:

- Three measures reported to Joint Commission

- Asthma Action Plan developed prior to discharge
- Length of Stay

Potential process measures:

- Use of Asthma Inpatient CPG Power Plan

Balancing measure(s):

- Rate of hospital asthma readmission within 7 days
- Adverse effects of IV magnesium sulfate for inpatients

Potential Cost Implications:

- Potentially decrease RT utilization as time to deliver albuterol by MDI spacer is less than by nebulizer
- Increase in assessment of proper MDI usage and targeted education on MDI/spacer technique resulting in:
  - Potential decrease in readmission because home administration of medication is more efficacious
  - Potential decrease in Emergency Department visits/readmissions because patients go home with an albuterol MDI/spacer that bridges the gap in the time between discharge and obtaining their albuterol prescription filled at their pharmacy

Potential Organizational Barriers:

- Reluctance of providers and Respiratory Therapists to change practice from the use of nebulizers (intermittent) to the use of MDI/spacer in the hospital setting
- Change in pharmacy practice/costs to obtain more MDIs and spacers and dispose of inhalers (regulations recently changed disposal to black diamond boxes) versus nebulizers which are disposed in regular trash

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Clinical Questions Answered:

Question 1: What level of oxygen saturation was used as a cutoff for initiation of supplemental oxygen for subjects in studies of asthma exacerbations?

Inpatient asthma team recommendation:
Based on moderate quality evidence, the inpatient asthma team strongly recommends using supplemental oxygen to keep the patient's oxygen saturation ≥ 90-92%. Pulse oximetry measurements are used to assess the severity of the exacerbation and the response to treatment. In infants and children, where the ability to perform FEV1 or PEF testing is diminished, monitoring SpO2 is essential. SpO2 less than 90-92% on room air is an indicator for hospitalization, therefore the goal is to keep SpO2 greater than or equal to 90-92% (EPR-3, 2007). The benefits of an oxygen saturation ≥ 90-92% outweigh undesirable effects. This recommendation applies to most patients in most circumstances. Further research (if performed) is likely to have an important effect on our confidence in the estimate of effect and may change the estimate.

Literature (see Appendix A) supporting this recommendation:
The literature since (EPR-3, 2007) was searched and no new research was found. Boychuk, Yamamoto, DeMesa, & Kiyabu (2006) was referenced to support EPR-3 (2007) (See Table 1). Colorado Children's Guideline (2011) states supplemental oxygen should be used for any child whose SpO2 is less than 90% and Cardinal Glennon's Guideline (2009) does not give guidance on this recommendation. Ten citations were read to establish the oxygen saturation level utilized to determine therapy (see Table 2).

Search strategy implemented:
PubMed performed February 26 2015:(There were no new citations that addressed the question since the 2010 search was performed).

("Asthma"[Mesh] AND ("Emergency Service, Hospital"[Mesh] OR "Emergency Nursing"[Mesh] OR "Emergency Medical Services"[Mesh] OR "Emergency Medicine"[Mesh] OR "Acute Disease"[Mesh] OR exacerbation[All Fields] OR attack[All Fields])) AND ("Oximetry"[Mesh] OR "permissive hypoxia"[All Fields]) AND ((Meta-Analysis[ptyp] OR Practice Guideline[ptyp] OR Randomized Controlled Trial[ptyp] OR Guideline[ptyp]) OR ("Cohort Studies"[Mesh] OR "Epidemiologic Studies"[Mesh] OR systematic[sb])) AND English[lang] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms])http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/public/10Wv9ymw-CX6RXeY07Yk-EXQz/

19 citations

CINAHL performed Sept 16, 2010:

S1 (MH "Acute Disease") **Limiters** - Exclude MEDLINE records **Search modes** - Boolean/Phrase
S2 (MH "Emergency Medical Services+") OR (MH "Emergency Service+") OR (MH "Emergency Nursing+") OR (MH "Emergency Medicine") **Limiters** - Exclude MEDLINE records **Search modes** - Boolean/Phrase. No citations

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Table 1
Synthesis of relevant literature about oxygen saturation values to guide treatment of children with acute asthma exacerbations

<table>
<tr><th>Author, date, country, and industry of funding</th><th>Patient Group</th><th>Level of Evidence</th><th>Research design</th><th>Significant results</th><th>Limitations</th></tr>
<tr><td>(Boychuk et al., 2006).</td><td>1219 encounters of 1008 unique children with acute asthma in 5 EDs/clinics, including urban, suburban, and rural settings.
Children were> 12 months and < 18 years, presenting with wheezing or bronchospasm.
Convenience enrollment</td><td>Low</td><td>Prospective cohort study.

Asthma severity was determined by NIH severity class groups.
Phase 1 subjects received usual care.
Phase 2 subjects received an educational video, and a written asthma action plan</td><td>Phase 1 and Phase 2 groups were similar except Phase 2 subjects were older. (Phase 1 mean age was 3.6 $\pm$ 2.3 and Phase 2 mean age was 4.3 $\pm$ 3.4 [p< 0.0001]).
The overall hospitalization rate was 15%.
The greater the severity classification, the higher the hospitalization rate.
The lowest severity group was least likely to have an asthma action plan.
Hospitalization rates by presenting oxygen saturation:
<table>
<tr><th>Presenting oxygen saturation</th><th>Admission rate</th></tr>
<tr><td>98% -100%</td><td>6%</td></tr>
<tr><td>95%-97%</td><td>12%</td></tr>
<tr><td>93%-94%</td><td>28%</td></tr>
<tr><td>90%-92%</td><td>45%</td></tr>
<tr><td>85%-89%</td><td>65%</td></tr>
<tr><td>80%-84%</td><td>100%</td></tr>
</table>
The mean O_2 saturation across severity scores ranged from 96.0 +3.0 to 96.8+2.5. There was no significance among initial O_2 saturation and severity score. Severity score was not related to admission rate.</td><td>Severity Score is a global score of asthma, not a measure of the event that brought the child to the ED. It is easy to confuse the term “severity score” in relation to the acute event versus the burden of the disease which the score measures.
The age difference between Phase 1 and Phase 2 subjects could be a concern for bias.
Some of the initial O_2 saturation measures may have been obtained with the subject receiving supplemental O_2.</td></tr>
</table>

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Table 2

Oxygen saturation level used to determine need for oxygen therapy in ten research papers and altitude of study location

	Saturated oxygen values	Locations altitudes
(Kelly, Kerr, & Powell, 2004)	Mild > 94%, Moderate 94-90% and Severe < 90%	36 Australian centers various altitudes
(Keogh et al., 2001)	Used a saturated oxygen of < 92% to administer supplemental oxygen	Toronto Canada, altitude: 105 m. (347 ft.)
(Sole, Komatsu, Carvalho, & Naspitz, 1999)	92% was the cut off predicting the necessity to repeat treatment	Sao Paulo Brazil, altitude: 637 ft.
(Wright, Santucci, Jay, & Steele, 1997)	Pretreatment saturated oxygen < 91% was not useful in predicting admission/relapse (sensitivity 0.24, specificity 0.86, likelihood ratio of 1.77) and Post treatment saturated oxygen < 91% had a sensitivity of 0.34 and a specificity of 0.98 with a likelihood ratio of 16.43 to predict admission/relapse.	Providence RI, altitude: 50 ft.
(Keahey et al., 2002)	The mean saturated oxygen of children admitted was 93 $\pm$ 5% and the mean saturated oxygen of children not admitted was 96% $\pm$ 3%	44 Emergencies 18 in US states and 4 Canadian provinces. Various altitudes
(Carruthers & Harrison, 1995)	Adults 32% were smokers	Norwich UK, altitude: 30 m. (28 ft.)
(Mehta, Parkin, Stephens, Keogh, & Schuh, 2004)	In the group (n= 107) that needed < 4 hours of frequent bronchodilator treatment (FBT) presenting saturated oxygen was 95.5 $\pm$ 2. In the group (n=166) that needed > 4 hours of FBT, presenting saturated oxygen was 93.3 $\pm$ 3.8	Toronto Canada, altitude: 105 m. (347 ft.)
(Boychuk et al., 2006)	Presenting saturated oxygen < 90 related to increased hospitalization	Honolulu, HI, altitude: 4 m. (9 ft.)

First Author, Year	Saturated oxygen values	Locations altitudes
(Connett & Lenney, 1993)	Inpatients 75, all were children. All children required nebulization therapy with salbutamol 5 mg. Only those who required hospitalization were included in the study. Oxygen saturation was measured prior to nebulization and 10 minutes post nebulization. Children were awake. All received prednisone 2 mg/kg, PO. A post nebulization oxygen saturation that was < 91% best predicted the need for IV treatment (IV aminophylline and hydrocortisone).	Brighton, UK altitude: 0 ft.
(Geelhoed, Landau, & LeSouef, 1994)	Subjects: 280 children who were enrolled when the primary investigator was working. 198 were receiving episodic treatment and 82 were receiving regular treatment, including 11 who were on regular oral steroids. Treated in the ED with nebulized salbutamol. A minority (n = unknown) were given oral steroids. Subjects with a poor outcome (admission to the hospital) had a mean oxygen saturation of 92.4%, SD 3.2%. Subjects with a good outcome (discharged from the ED) had a mean oxygen saturation of 95 %, SD 2.0%.	Perth, Western Australia altitude: 66 ft.

Question 2: What are the maximum doses of continuous albuterol?

Inpatient asthma team recommendation:

EPR-3 (2007) recommends the following dosages for intermittent and continuous albuterol:

- Child dose (≤ 12 years of age)—0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses then 0.15 to 0.3 mg/kg up to 10 mg every 1 to 4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization with a maximum of 10 mg/hour continuously.
- Adult dose (> 12 years of age)—2.5 to 5 mg every 20 minutes for 3 doses, then 2.5 to10 mg every 1 to 4 hours as needed, or 10 to 15 mg/hour continuously.

EPR-3 (2007) recommends only selective beta2-agonists (albuterol, levalbuterol, pirbuterol). For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6–8 L/min. Use large volume nebulizers for continuous albuterol administration. The inpatient asthma team concurs with these recommendations, including the use of 15 mg/hour as the maximum dose per hour of continuous albuterol. The inpatient asthma team values amelioration of symptoms while minimizing adverse effects of the medication. This is a strong recommendation based on high quality evidence (EPR-3, 2007).

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Question 3: **In the child hospitalized with an asthma exacerbation, should intravenous fluids be routinely administered?**

Inpatient asthma team recommendation:

EPR-3 (2007) does not recommend routine intravenous fluids for older children with asthma. The assessment of the hydration status of patients will guide the decision to start intravenous fluids. In young children, an increased respiratory rate coupled with decreased oral intake, may put the child at risk for dehydration.

Literature (Appendix B) supporting this recommendation:
An extensive literature search was performed and was not successful in finding information to answer this specific question.

Search strategy implemented:
PubMed search performed December 20 2011, and repeated February 26 2015, no new citations were identified.
"asthma"[All Fields] AND ("Fluid Therapy"[Mesh] OR "Infusions, Parenteral"[Mesh] OR "Saline Solution, Hypertonic"[Mesh] OR "Hypotonic Solutions"[Mesh] OR "Isotonic Solutions"[Mesh] OR "Water-Electrolyte Balance"[Mesh] OR "Water-Electrolyte Imbalance"[Mesh] OR "Rehydration Solutions"[Mesh]) AND ((Meta-Analysis[ptyp] OR Practice Guideline[ptyp] OR Randomized Controlled Trial[ptyp] OR Guideline[ptyp] OR "Comparative Study"[Publication Type] OR "Controlled Clinical Trial"[ptyp]) OR ("Cohort Studies"[Mesh] OR systematic[sb])) NOT (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp] OR Case Reports[ptyp]) AND English[lang] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms]) AND ("2001/12/31"[PDat] : "2011/12/28"[PDat])

34 citations

Question 4: In the child hospitalized with an asthma exacerbation, should intravenous magnesium sulfate be used to improve pulmonary function?
Question 5: **In the child hospitalized with an asthma exacerbation, should more than one treatment with intravenous magnesium be given?**

Inpatient asthma team recommendation:
Based on very low quality evidence, the inpatient asthma team recommends the consideration of IV magnesium sulfate for children hospitalized for a severe asthma exacerbation if conventional therapy is failing and it has not been already given.

Based on very low quality evidence we recommend considering the administration of intravenous magnesium for children with moderate asthma exacerbations that have failed to respond to continued therapy after one hour. Research performed in adults has shown beneficial effects of magnesium given to adult patients seen in the Emergency Department for asthma exacerbations.

Additionally, no literature was found to answer the question about providing more than one dose of magnesium sulfate. We cannot recommend for or against multiple doses of magnesium when treating hospitalized patients with asthma exacerbations. We place a high value on using therapies with known efficacies. Further research (if performed) is likely to have an important effect on our recommendation.

Literature (Appendix C):
No literature was found regarding the use of IV magnesium in children hospitalized for asthma exacerbations. However, for adult patients seen in the Emergency Department, administration of intravenous magnesium has been shown to significantly improve respiratory function as measured by PEFR (% predicted) and asthma score. SMD 1.94, 985% CI [0.8, 3.08] (Mohammed & Goodacre, 2007). This evidence is graded as very low quality based on three factors.

1. The evidence does not directly apply to hospitalized children; all studies were completed in the ED.
2. The findings are imprecise. The number of subjects in the in the meta- analysis is 128 total subjects.
3. The outcome PEFR is difficult to measure in children < 5 years. It is unknown if the children were able to adequately perform the maneuver to obtain this outcome.

Torres et al. (2012) reported a significant reduction in use of mechanical ventilation when IV magnesium sulfate (25 mg/kg, maximum 2 grams over 20 minutes) was administered to children aged 2-15 years within the first hour of presentation of a severe asthma attack (Wood's score >/= 5) (See Figure 1).

We did not find any evidence to support or refute more than one treatment with IV magnesium sulfate.

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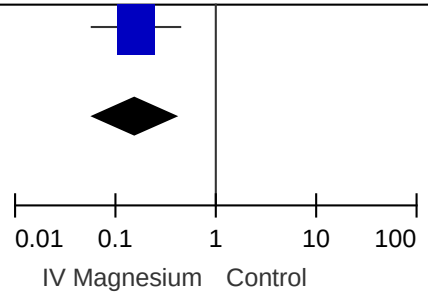
Forest Plot comparison

Study or Subgroup	IV Magnesium Events	IV Magnesium Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Torres 2012	4	76	22	67	100.0%	0.16 [0.06, 0.44]
Total (95% CI)		**76**		**67**	**100.0%**	**0.16 [0.06, 0.44]**
Total events	4		22			

Heterogeneity: Not applicable

Test for overall effect: Z = 3.54 (P = 0.0004)



Risk of bias legend

(**A**) Random sequence generation (selection bias)

(**B**) Allocation concealment (selection bias)

(**C**) Blinding of participants and personnel (performance bias)

(**D**) Blinding of outcome assessment (detection bias)

(**E**) Incomplete outcome data (attrition bias)

(**F**) Selective reporting (reporting bias)

(**G**) Other bias

Figure 1. Intravenous magnesium sulfate vs. control in Severe Asthma, Outcome: Need for mechanical ventilation

Question 6: In the child hospitalized with an asthma exacerbation, should albuterol be administered by nebulizer or metered-dose inhaler (MDI) and spacer to improve pulmonary function?

Inpatient asthma team recommendation:
EPR-3 (2007) makes no statement of preference of using a nebulizer over an MDI with a valved spacer for the administration of inhaled medications. In addition, they conclude "it is important to assess inhaler techniques for all prescribed medications and reinforce correct technique before patients are discharged home." Thus, based on studies conducted in Emergency Departments for children with mild-to-moderate exacerbations, administration of inhaled medications via an MDI plus valved holding chamber is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel. A mask should be used for children < 4 years of age. Nebulized albuterol should be reserved for children with moderate-to-severe symptoms. We placed high value on prompt resolution of symptoms and the ability to evaluate the patient's technique when using an MDI and spacer.

Literature:
Literature was not found to support using MDI with spacer versus nebulizer for the delivery of albuterol for children hospitalized with asthma exacerbation.

Search strategy:
(("Asthma"[Mesh] AND ("Emergency Service, Hospital"[Mesh] OR "Emergency Nursing"[Mesh] OR "Emergency Medical Services"[Mesh] OR "Emergency Medicine"[Mesh] OR "Acute Disease"[Mesh] OR exacerbation[All Fields] OR attack[All Fields])) AND ("Magnesium Sulfate"[Mesh]

Question 7: In the child hospitalized with an asthma exacerbation, should methylprednisolone/ prednisolone/prednisone vs. dexamethasone be used to improve pulmonary function?

Inpatient asthma team recommendation:
Based on high quality evidence, we recommend a 5-day course of oral prednisolone/prednisone for acute asthma exacerbations. The National guideline (EPR-3, 2007) states dexamethasone is not preferred due to the increased duration of drug activity that increases the risk of adrenal suppression. For this recommendation, we placed a high value on decreasing unscheduled re-evaluations, re- admissions, and cost of treatment.

Literature (see Appendix D) supporting this recommendation:
Since EPR-3 (2007) a meta- analysis of six studies by Keeney et al. (2014) reported that relapse rate at 5 days and 10-14 days post treatment for asthma exacerbation were similar for children treated with dexamethasone or prednisolone/prednisone. The forest plots of the studies included in Keeney are included in Figures 2 and 4. In addition, they reported that vomiting was significantly less in the groups treated with dexamethasone. GRADing the Keeney et al., (2014) paper shows the following (see Tables 3 and Table 4).

For the vomiting comparison, treatment with dexamethasone was intramuscular in three of the four studies, while treatment with prednisolone/prednisone was PO in all studies. Prednisolone/prednisone doses were either singular or multiple oral doses

1. Doses of corticosteroids varied widely across studies:
   - The dose of IM dexamethasone ranged from 0.3 mg/kg with a mix of 15 mg IM X 1 dose to 1.7 mg/kg (max 36 mg) IM X 1 dose. The range of oral dexamethasone ranged from 0.3 mg/kg (max 15 mg) PO X 1 dose to 0.6 mg/kg (max 16 mg) PO once daily X 2 days.
2. The studies were not powered on the outcome vomiting.

Therefore, the asthma inpatient team does not recommend the use of dexamethasone over prednisolone/prednisone at this time. Future research will change our confidence in the estimate of the effect.

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Tables

TABLE 3
*GRADE assessment of studies included in (Keeney et al., 2014)***.**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**In-consistency**	**Indirect-ness**	**Imprecision**	**Other considerations**	**Dexamethasone**	**Prednisone**	**Relative (95% CI)**	**Absolute**		
Vomiting in the ED (follow-up 2-4 hours)												
4	randomized trials	serious[1,2]	serious[3,4]	no serious indirectness	serious[5]	none	6/506 (1.2%)	27/511 (5.3%)	OR 0.18 (0.07 to 0.45)	43 fewer per 1000 (from 27 fewer to 49 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Relapse rate - 5 days (follow-up 5 days; assessed with: number who returned for treatment of the exacerbation)												
4	randomized trials	serious[1,2]	serious[3,4]	no serious indirectness	serious[5]	none	14/167 (8.4%)	15/169 (8.9%)	OR 0.96 (0.43 to 2.11)	3 fewer per 1000 (from 49 fewer to 82 more)	⨁◯◯◯ VERY LOW	CRITICAL
Relapse rate - 10-15 days (follow-up 10-14 days; assessed with: number who returned for treatment of exacerbation)												
3	randomized trials	serious[1,2]	serious[3,4]	no serious indirectness	serious[5]	none	47/391 (12%)	40/372 (10.8%)	OR 1.18 (0.74 to 1.87)	17 more per 1000 (from 26 fewer to 76 more)	⨁◯◯◯ VERY LOW	CRITICAL

[1] There is poor reporting of allocation concealment in half of the studies.
[2] One third of the studies blinded the participants, and in only one study were outcome assessors blinded.
[3] The I2 statistic low (0- 18.7) but there were differences in the treatments, 3 studies used a single IM dose of dexamethasone, 1 study used a single oral dose and 2 studies used multiple oral doses.
[4] The dose of IM dexamethasone ranged from 0.3 mg/kg with a maximum of 15 mg IM X 1 dose to 1.7 mg/kg 1.7 mg/kg (max 36 mg) IM X 1 dose. The range of oral dexamethasone ranged from 0.3 mg/kg (max 15 mg) PO X 1 dose to 0.6 mg/kg (max 16 mg) PO once daily X 2 days.
[5] Low number of subjects and low number of events

Table 4

Dose and duration of Intervention and Comparison of the studies included in Keeney et al., (2014)

Author	Intervention	Comparison
Single IM dose		
(Gries, Moffitt, Pulos, & Carter, 2000)	Dexamethasone 1.7 mg/kg (max 36 mg) IM X 1 dose	Prednisone or prednisolone 1 mg/kg (max 20 mg) PO twice daily X 5 days
(Gordon, Tompkins, & Dayan, 2007)	Dexamethasone 0.6 mg/kg (max 15 mg) IM X 1 dose	Prednisolone 2 mg/kg (max 50 mg) PO daily X 5 days
(Klig, Hodge, & Rutherford, 1997)	Dexamethasone 0.3 mg/kg (max 15 mg) IM X 1 dose	Prednisone 2 mg/kg (max 100 mg) PO X 1 dose, then 1 mg/kg PO daily X 2 days
Single Oral Dose		
(Altamimi et al., 2006)	Dexamethasone 0.6 mg/kg (max 18 mg) PO X 1 dose, then placebo PO twice daily for 5 days	Prednisone or prednisolone 1 mg/kg (max 30 mg) PO X 1 dose, then 1 mg/kg PO twice daily X 5 days
Multiple Oral Dose		
(Greenberg, Kerby, & Roosevelt, 2008)	Dexamethasone 0.6 mg/kg (max 16 mg) PO once daily X 2 days	Prednisone 2 mg/kg (max 80 mg) PO X 1 dose, then 1 mg/kg(max 30 mg) PO twice daily X 4 days
(Qureshi, Zaritsky, & Poirier, 2001)	Dexamethasone 0.6 mg/kg (max 16 mg) PO once daily X 2 days	Prednisone or prednisolone 2 mg/kg (max 60 mg) PO X 1 dose, then 1 mg/kg (max 60 mg) PO daily X 4 days

Figures

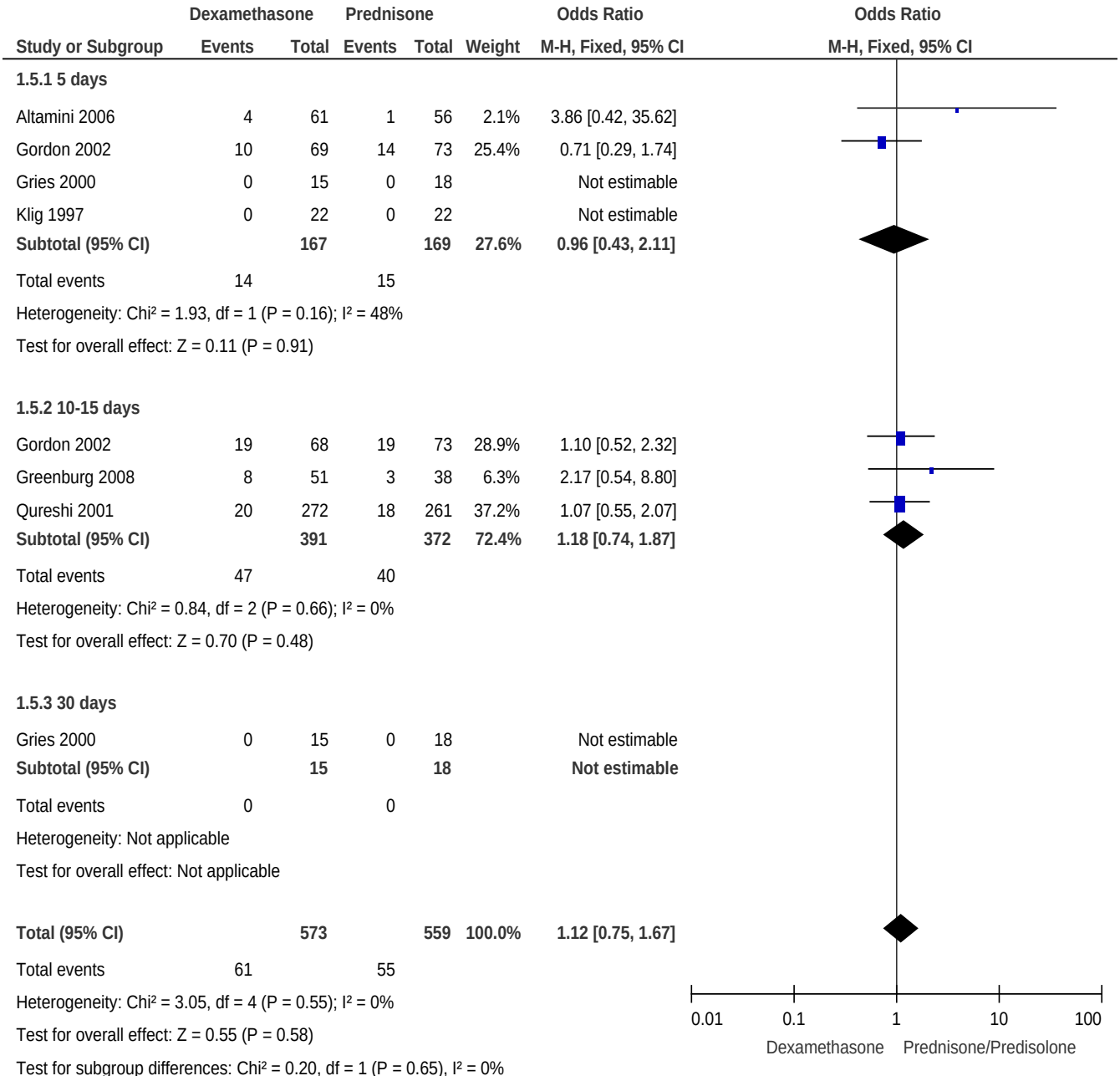

Figure 2. Dexamethasone vs. Prednisone/prednisolone, Outcome Relapse. All studies except Gordon et al. (2007) compare administration by mouth. Gordon et al. (2007) compared dexamethasone intramuscularly vs. prednisone/prednisolone by mouth.

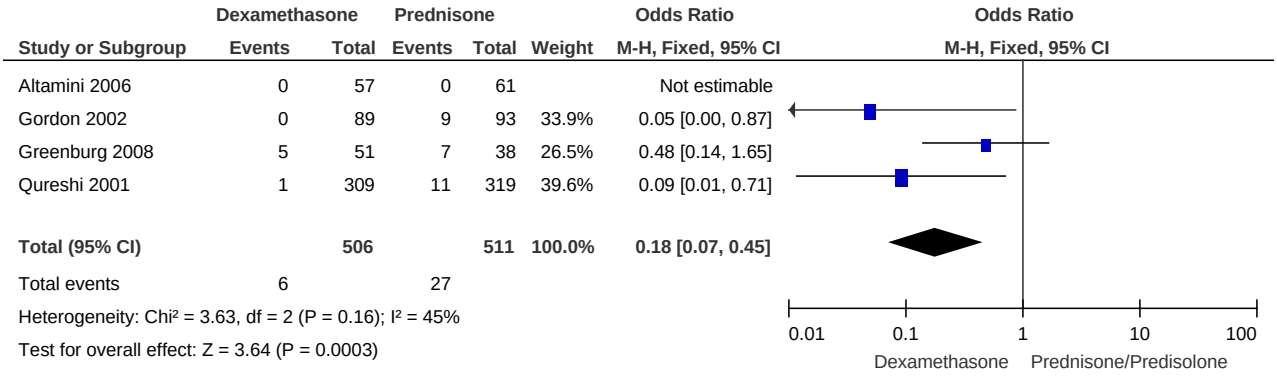

Figure 3. Dexamethasone vs. Prednisone/Prednisolone, Outcome Vomiting in the ED. All studies except Gordon et al., (2007) compare administration by mouth. Gordon et al., (2007) compared dexamethasone intramuscularly vs. prednisone/prednisolone by mouth.

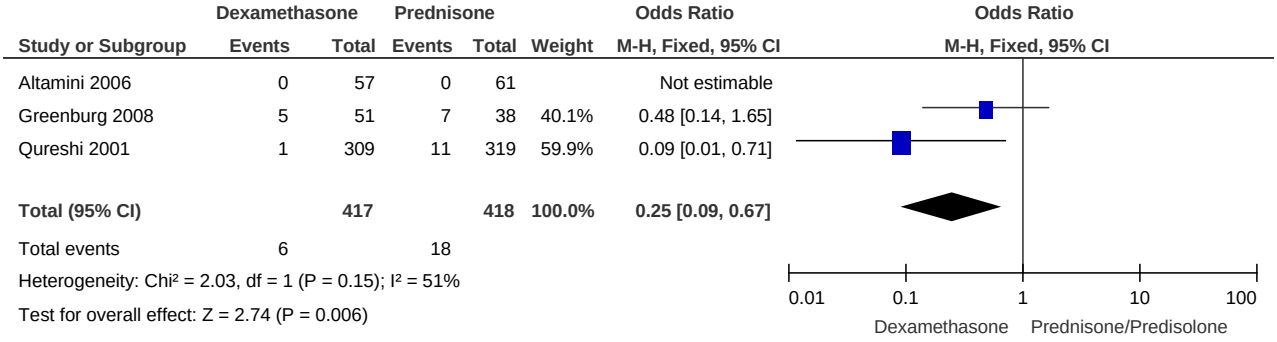

Figure 3[a]. Dexamethasone vs. Prednisone/Prednisolone, Outcome Vomiting in the ED (Gordon et al., 2007)

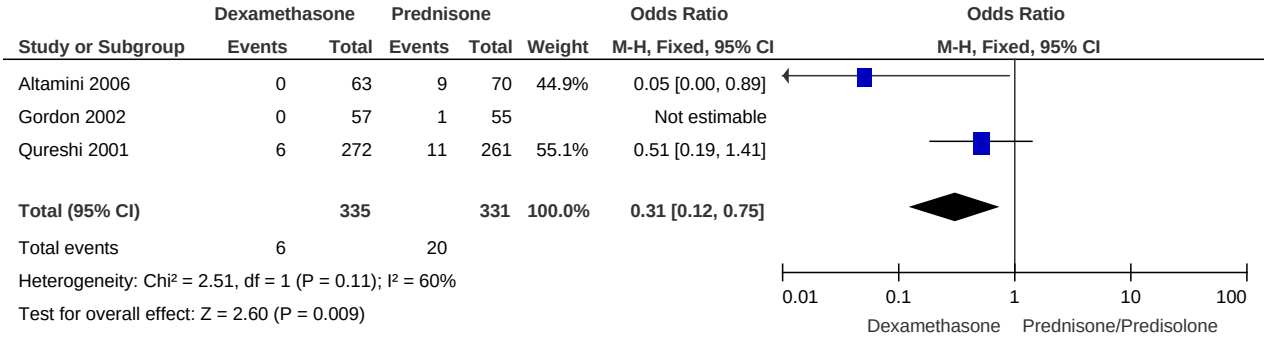

Figure 4. Dexamethasone vs. Prednisone/Prednisolone, Outcome Vomiting at home. All studies except Gordon et al., (2007) compare administration by mouth. Gordon et al., (2007) compared dexamethasone intramuscularly vs. prednisone/prednisolone by mouth.

Question 8: In the child hospitalized with an asthma exacerbation, should inhaled steroids be initiated during an asthma exacerbation to improve pulmonary function or should inhaled corticosteroids be continued if the treatment is included on the child's home Asthma Action Plan (AAP)?

Inpatient Asthma Team Recommendation:

We recommend starting or continuing an inhaled corticosteroid (ICS) in children hospitalized for an asthma exacerbation. We do not recommend treating an asthma exacerbation with inhaled corticosteroids ONLY. Doubling the AAP dose of ICS at the onset of an exacerbation is not recommended. However, starting or continuing ICS for an inpatient with an asthma exacerbation theoretically allows a foundation for assuring compliance with the AAP after discharge (Edmonds, Milan, Brenner, Camargo, & Rowe, 2012; EPR-3, 2007; Rowe, Edmonds, Spooner, Diner, & Camargo, 2004), although this has not been studied.

Literature supporting this recommendation:

EPR-3 (2007) makes the following statements:

> Doubling the dose of the ICS does not appear to be effective (FitzGerald et al., 2004); Garrett, Williams, Wong, & Holdaway, 1998; Harrison, Oborne, Newton, & Tattersfield, 2004). Multiple high doses of an ICS (6 mg flunisolide over 3 hours) may be helpful in adults.

In children, the data is inconsistent (Rowe et al., 2004) most likely due to inconsistency in study designs. A meta-analysis by (Edmonds et al., 2012)in a primarily adult population that compared ICS vs. oral steroid and ICS, there was no significant difference in the odds ratio (OR) for asthma relapse at 7-10 days post treatment OR = 0.72, 95% CI [0.48, 1.1] and hospital admission OR = 0.99, 95% CI [0.39, 2.52].

Question 9: In the child hospitalized with an asthma exacerbation, should positive expiratory pressure (PEP) therapy be used?

Inpatient Asthma team recommendation:
Based on very low quality evidence the Asthma Inpatient CPG team makes a weak recommendation that PEP therapy may be used in the treatment of children hospitalized with asthma. Due to the lack of evidence on this therapy, a strong quality project or research study should be done to understand the efficacy of the treatment. Other alternatives may be equally reasonable. Further research (if performed) is likely to have an important influence on our confidence in the estimate of the effect and is likely to change the estimate.

Literature (Appendix E):
The literature was searched since the publication of EPR-3 (2007). Two studies were identified. The studies are reported individually because the comparisons and outcomes differ for each study. Christensen, Norregaard, Jensen, & Dahl 1993) compared β2-agonists and PEP with functional residual capacity (FRC) and airway resistance (RAW). Frischknecht-Christensen, Norregaard, & Dahl (1991) used the same comparison but measured peak expiratory flow (PEF) and forced expired volume (FEV). Neither study showed improvement in the measured outcomes using PEP therapy. Clinical experience at Children's Mercy has shown the usefulness of PEP therapy in children with asthma. Texas Children's Hospital and Denver Children's Hospital were contacted regarding the use of PEP therapy in hospitalized children with asthma. Texas Children's does not use PEP routinely and Denver Children's uses EzPAP, not PEP, due to the lack of evidence.

Forest Plot Comparisons

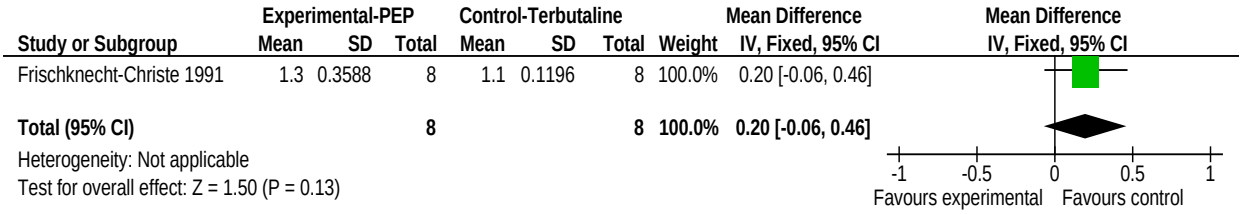

Figure 5. PEP versus Terbutaline, Outcome Symptom Score

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