

**TEXAS CHILDREN'S HOSPITAL**  
**EVIDENCE-BASED OUTCOMES CENTER**  
**Asthma/Recurrent Wheezing Clinical Guideline**  
Evidence-Based Guideline

**Definition:** <sup>(1)</sup> Acute asthma exacerbations or “asthma attacks” are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms. Respiratory distress is common. Exacerbations are characterized by decreases in expiratory airflow that can be quantified by measurement of lung function (PEF or FEV<sub>1</sub>).

**Pathophysiology:** <sup>(2)</sup> Asthma is a complex process that depends on the interaction of:

- Bronchoconstriction
- Airway hyperresponsiveness
- Airway inflammation, resulting in edema and mucus plugging

**Inclusion Criteria**

- Patients ≥2 years with a diagnosis of asthma/recurrent wheezing in whom foreign body or vocal cord dysfunction have been ruled out

**Exclusion Criteria**

- Other chronic lung disease, bronchiolitis, bacterial pneumonia, neurological disorders, immunodeficiency diseases, and cardiac patients

**Differential Diagnosis** <sup>(1,2)</sup>

Foreign body	Croup
Heart failure	Vocal cord dysfunction
GERD	

**Diagnostic Evaluation**

**History of the Exacerbation: Assess for** <sup>(1-3)</sup>

- Severity and duration of symptoms, including exercise limitation and sleep disturbance
- All current medications, including dose (and device) prescribed, dose usually taken, frequency, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy
- Time of onset and cause of the present exacerbation
- Risk factors for asthma-related death
- Level of control

**History of Disease: Assess for** <sup>(2)</sup>

- Patient/Family history of asthma, eczema, and/or smoking
- Patient history of allergic rhinitis, sinusitis, nasal polyps, eczema, or BPD
- Recurrent cough, bronchitis, or bronchiolitis
- Cough, wheeze, shortness of breath, and/or chest tightening that occurs in an “episodic” fashion. These symptoms may occur or worsen with:
  - Exercise
  - Weather change
  - Nighttime hours
  - Viral infection
  - Inhalant exposure (e.g., smoke, fur, dust mites, mold, pollen)
  - Irritant exposure (e.g., airborne chemicals, smoke)
  - Strong emotions (e.g., laughing, crying)
  - Menstrual cycle

**Physical Examination** <sup>(2)</sup>

- Evaluate patient's ability to complete a sentence
- Pulse rate
- Respiratory rate
- Use of accessory muscles
- Severity of respiratory symptoms using the Clinical Respiratory Score (CRS)
- Rhinitis, increased nasal secretions, mucosal swelling, or nasal polyps

**Exacerbation Severity Assessment Tool**

<b>Clinical Respiratory Score (CRS)</b>			
Assess	Score 0	Score 1	Score 2
<b>Respiratory Rate</b>	<2 mos: <50 2-12 mos: <40 1-5 yrs: <30 >5 yrs: <20	<2 mos: 50-60 2-12 mos: 40-50 >1-5 yrs: 30-40 >5 yrs: 20-30	<2 mos: >60 2-12 mos: >50 >1-5 yrs: >40 >5 yrs: >30
<b>Auscultation</b>	Good air movement, scattered expiratory wheezing, loose rales/crackles	Depressed air movement, inspiratory and expiratory wheezes or rales/crackles	Diminished or absent breath sounds, severe wheezing, or rales/crackles, or marked prolonged expiration
<b>Use of Accessory Muscles</b>	Mild to no use of accessory muscles, mild to no retractions, no nasal flaring on inspiration	Moderate intercostal retractions, mild to moderate use of accessory muscles, nasal flaring	Severe intercostal and substernal retractions, nasal flaring
<b>Mental Status</b>	Normal to mildly irritable	Irritable, agitated, restless	Lethargic
<b>Room Air SpO<sub>2</sub></b>	>95%	90-95%	<90%
<b>Color</b>	Normal	Pale to normal	Cyanotic, dusky

(Add score from all rows to calculate total CRS score)

**Risk factors for asthma-related death include:**

- Comorbid conditions such as heart or lung disease
- Previous severe exacerbation (e.g., intubation or ICU admission)
- ≥2 hospitalizations or >3 EC visits within the past year
- Use of >2 canisters of short-acting beta-agonist (SABA) per month
- Difficulty perceiving airway obstruction or the severity of worsening asthma (parent and/or child)
- Low socioeconomic status or inner-city residence
- Illicit drug use
- Major psychosocial problems or psychiatric disease

**Life-threatening asthma involves a constellation of symptoms, including:**

- Marked chest tightness
- Wheezing, severe shortness of breath
- Retractions
- Cyanosis
- Inability to speak or speak in sentences due to dyspnea
- Hunched posture
- Altered mental status (agitation, anxiety, lethargy)

**Critical Points of Evidence\*****Evidence Supports**

- The Clinical Respiratory Score (CRS) should be used to determine the level of exacerbation severity. (4-7, Unpublished TCH data) – Strong recommendation, moderate quality evidence
  - Pulse oximetry should be used as part of the CRS to determine the level of exacerbation severity. (1,8,9) – Strong recommendation, low quality evidence
  - Blood gases should be used in the critical care setting to determine the level of exacerbation severity. (1,2,3,10,11,12) – Weak recommendation, low quality evidence
  - Dexamethasone should be given orally in the Emergency Department (ED) and in the inpatient setting and should be administered immediately during a moderate to severe exacerbation. (1,3,13-32) – Weak recommendation, moderate quality evidence
- Remarks:  
For children with a recent (within 1-2 weeks) course of steroids, history of ICU admission, or severe persistent asthma, consider a longer course of oral steroids for asthma exacerbations.  
Dexamethasone tablets are easily dissolvable, up to 16 mg in 1 mL of liquid (e.g., juice, water, sports drink). IV for PO solution is not available in outpatient pharmacies.
- Prednisolone/Prednisone should be given orally in the ambulatory setting. (1,3,13-32) – Weak recommendation, moderate quality evidence
  - Immediately administer SABA via metered-dose inhaler (MDI) for children with mild to severe asthma, reserving continuous SABA only for children requiring administration more than every 1 hour and for children with life-threatening asthma. (2,3,33-36) – Strong recommendation, moderate quality evidence
  - Either albuterol or levalbuterol should be used for SABA administration via MDI. (1,3,37-42) – Strong recommendation, moderate quality evidence
  - Albuterol should be used for SABA administration via nebulizer. Nebulized levalbuterol is an equally effective alternative but is much more expensive than nebulized albuterol. (37-42) – Strong recommendation, moderate quality evidence
  - Ipratropium bromide should be used with beta-agonist for three doses as adjunct therapy in children with moderate to severe asthma exacerbations. (1-3,43-46) – Strong recommendation, high quality evidence
  - IV magnesium sulfate should be used as adjunct therapy when there is inadequate response to conventional therapy within the first hour in children with moderate to severe asthma exacerbations. (47-50) – Strong recommendation, moderate quality evidence
  - IV terbutaline should be used in a monitored care setting for the treatment of children with severe asthma exacerbations. (51) – Weak recommendation, low quality evidence
  - Non-invasive positive pressure ventilation should be used prior to intubation in children with severe asthma exacerbations. (52-56) – Strong recommendation, low quality evidence
  - Tailored educational interventions should be delivered to all patients seen at TCH. (55-66) – Strong recommendation, high quality evidence
  - All patients seen at TCH should be given a written asthma action plan. (3,65-68) – Strong recommendation, high quality evidence
  - Discharge patients from the IP setting once the child has successfully completed every three-hour SABA X 2. (3,69-71) – Strong recommendation, low quality evidence
  - Refer any patient with an asthma exacerbation and high ED usage ( $\geq 4$  visits/year), severe asthma, or previous ICU admission to an asthma specialist, if not already done. (1,72,73) – Strong recommendation, low quality evidence
  - **Consider** referring any patient admitted to the hospital for an asthma exacerbation to an asthma specialist (to be seen within 4-6 weeks of discharge), if not already done. (1,72,73) – Weak recommendation, low quality evidence
  - Refer any patient admitted to the ICU for an asthma exacerbation to an asthma specialist (to be seen within 4-6 weeks of discharge), if not already done. (1,72,73) – Strong recommendation, low quality evidence

**Evidence Against**

- Spirometry should not be used routinely to determine the level of exacerbation severity, except in select cases (obesity and vocal cord dysfunction). Spirometry may have a role in the management of the patient later in the hospital course. (74,75) – Strong recommendation, low quality evidence
- Peak expiratory flow measurements should not be used to determine the level of exacerbation severity, except in patients with established use. (76,77) – Strong recommendation, low quality evidence
- Chest radiographs should not be used to determine the level of exacerbation severity. (1-3,78-80) – Strong recommendation, moderate quality evidence
- End tidal carbon dioxide (ETCO<sub>2</sub>) measurements should not be used to determine the level of exacerbation severity. (81,82) – Strong recommendation, low quality evidence
- Heliox should not be used in the treatment of children with asthma exacerbations. (3,83,84) – Strong recommendation, low quality evidence
- Subcutaneous terbutaline or epinephrine should not be used in the treatment of children with asthma exacerbations. (85-91) – Strong recommendation, low quality evidence
- Serum potassium levels should not be checked routinely in patients with no other underlying conditions that would worsen the effect of hypokalemia. (10,12,92-96) – Strong recommendation, moderate quality evidence

**Evidence Lacking/Inconclusive**

- Utilize standard-dose (40 mg/kg/dose) magnesium infusion (vs. high-dose) when magnesium infusion is required. (2,13-15,97-103) – Consensus recommendation
- Administer oxygen to maintain SpO<sub>2</sub>  $\geq 90\%$ ; however, transiently lower levels may be acceptable in patients who are otherwise ready for discharge. – Consensus recommendation
- Discontinue long-acting beta-agonists when short-acting beta-agonists are required more often than four-hourly. (3) – Consensus recommendation

- Send all patients admitted to the hospital for an asthma exacerbation for a follow-up with their PCP within 1 week of discharge. – Consensus recommendation
- There is insufficient evidence to address the following topics: Continuation or no continuation of LABA for patients admitted to observation or inpatient status, impact of cohorting asthma inpatients or having an asthma unit, <sup>(87)</sup> doubling the dose of inhaled corticosteroid at the first signs of an exacerbation (prehospital), <sup>(104,105)</sup> administration of 1 dose of dexamethasone vs. 2 doses for an asthma exacerbation, <sup>(17,20,24,30,31,106)</sup> or the standard practice of administering IV fluids along with magnesium sulfate to prevent hypotension. <sup>(14,15)</sup>

\*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

### **Condition-Specific Elements of Clinical Management**

**General:** The child's age and severity of illness are important factors to consider in diagnosing and managing an acute asthma exacerbation.

**Treatment Recommendations**  
**Exacerbation Management (see Respiratory Assessment and Management Protocol [RAMP], p. 5):**

#### **Emergency Center**

1. Obtain brief history, perform physical exam, and assess exacerbation severity using the CRS (p. 1). <sup>(4-7)</sup>
2. Administer oxygen to maintain SpO<sub>2</sub> ≥90%. Transiently lower levels may be acceptable in patients who are otherwise ready for discharge.
3. Initiate SABA (levalbuterol or albuterol via MDI or albuterol via nebulizer, depending on severity). <sup>(1-3,33-42)</sup>
4. Consider/Administer dexamethasone. <sup>(1,3,17,18,20-22,29,32)</sup>
5. If severity warrants, consider/add ipratropium bromide (up to 3 doses). <sup>(1-3,43-46)</sup>
6. If there is inadequate response within the first hour of conventional therapy, consider/administer IV magnesium sulfate. <sup>(47-50)</sup>
7. If condition unchanged or worsening, consider initiation of adjunct therapies, including IV terbutaline and non-invasive positive pressure ventilation (NPPV), and admit to PICU. <sup>(51-56)</sup>
8. If condition unchanged or slightly improving but continued close monitoring is required, consider IP admission.
9. If condition has improved greatly, wean SABA, complete Asthma Action Plan (see Table 1 on p. 4 for additional guidance), and discharge home. <sup>(3,65-68)</sup>

#### **PICU**

1. Continue above and consider adjunct therapies yet to be initiated.
2. Consider intubation and mechanical ventilation as needed.
3. Continue to reassess. When improving, refer to RAMP and follow to discharge.

#### **Inpatient**

1. Begin discharge process upon admission.
2. Continue therapies and wean as appropriate according to RAMP.
3. Administer flu shot, if not already given. <sup>(107)</sup>
4. Complete Asthma Action Plan (see Table 1 on p. 4 for additional guidance) and discharge home once discharge criteria are met. <sup>(3,65-68)</sup>

#### **Admission Criteria**

- Oxygen saturation consistently <90%
- CRS ≥4
- Unsafe to send home/poor follow-up

#### **Discharge Criteria**

- No oxygen requirement
- CRS ≤3
- Response sustained at least 1-3 h after last SABA (EC) OR SABA q3h X 2 (Inpatient)
- Asthma Action Plan given
- Asthma Education complete
- Appropriate support system (e.g., PCP, caregivers)

#### **Referrals/Follow-Up Care**

- Patients admitted to the hospital for an asthma exacerbation should be seen by their PCP within 1 week of discharge.
- **Consider** referring patients admitted to the hospital with an asthma exacerbation to an asthma specialist (to be seen within 4-6 weeks of discharge), if not already done. <sup>(72,73)</sup>
- Refer any patient admitted to the ICU for an asthma exacerbation to an asthma specialist (to be seen within 4-6 weeks of discharge), if not already done. <sup>(1,72,73)</sup>
- Refer patients with high ED usage (≥4 visits/year), severe asthma, or previous ICU admission to an asthma specialist. <sup>(72,73)</sup>
- Criteria for referral to the Life-Threatening Asthma (LTA) Clinic:
  - PICU admission
  - On ventilator at any time
  - Very high ED usage without admission (≥5 visits/year)
  - Admission to the floor/TICU >2 times in past 18 months
  - History of asthma complication (e.g., loss of consciousness, seizure, cardiopulmonary arrest)
- Smoking cessation information should be given to patients, parents, and/or caregivers who are smokers.

#### **Balanced Scorecard Measures**

##### **Process**

- Time from ED arrival to delivery of beta-agonist
- Proportion of patients with a chest x-ray obtained
- Proportion of patients who received an Asthma Action Plan
- Proportion of patients filling controller medications

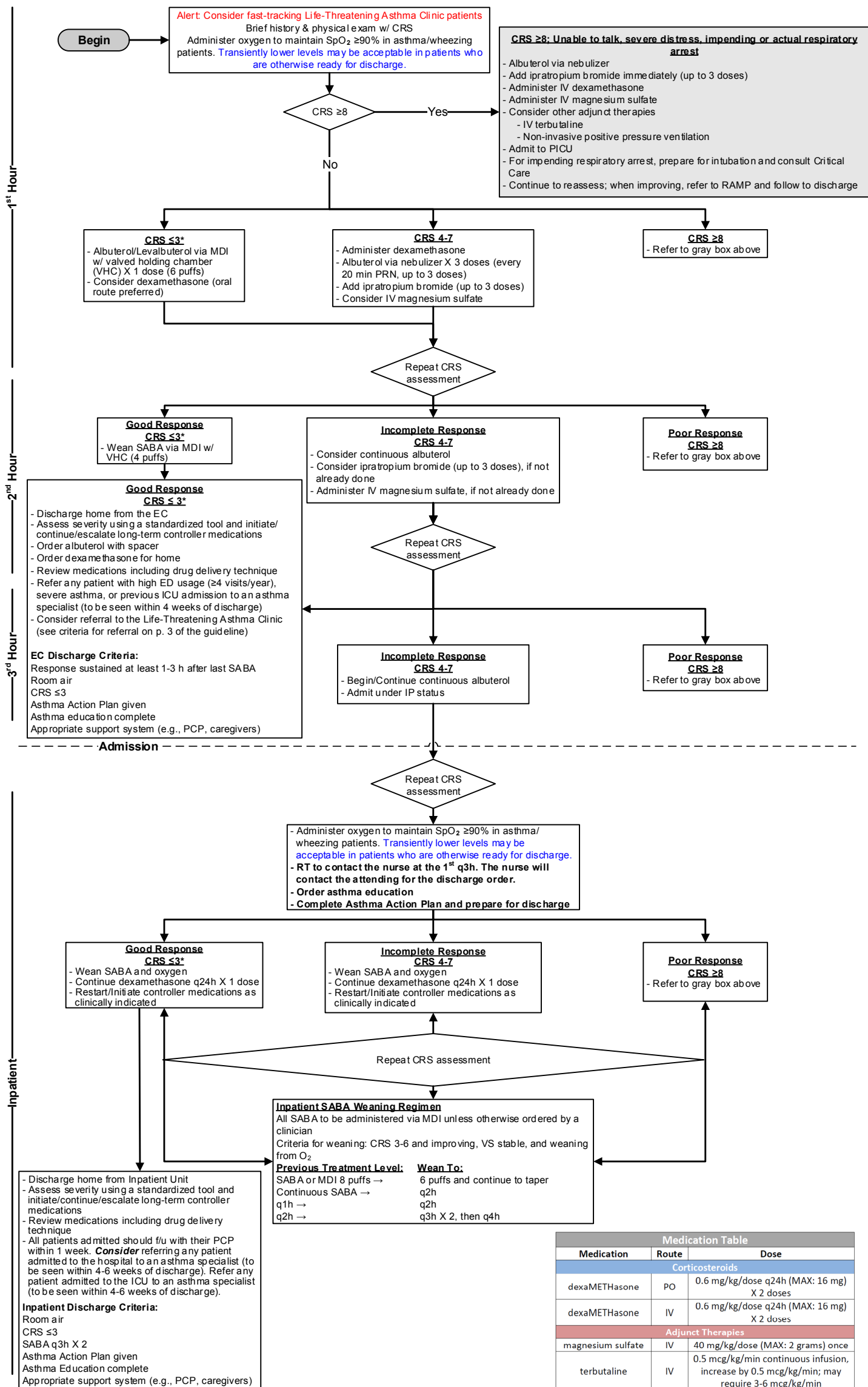
##### **Outcome**

- Readmission rate to the ED and inpatient

**Table 1. Classifying Asthma Severity and Initiating Therapy <sup>(2)</sup>**

	<b>Intermittent</b>	<b>Mild Persistent</b>	<b>Moderate Persistent</b>	<b>Severe Persistent</b>
<b>Symptoms</b>	≤2 days/week	>2 days/week	Daily	Throughout the day
<b>Nighttime awakenings</b>	0 (≤4 years) ≤2x/month (≥5 years)	1-2x/month (≤4 years) 3-4x/month (≥5 years)	3-4x/month (≤4 years) >1x/week (≥5 years)	> 1x/week (≤4 years) Often 7x/week (≥5 years)
<b>SABA use</b>	≤2 days/week	>2 days/week	Daily	Several times/day
<b>Activity limitation</b>	None	Minor	Some	Extreme
<b>Oral steroid usage</b>	0-1x/year	≥2x in 6 months or ≥4x/year (≤4 years) ≥2x/year (≥5 years)		
<b>Recommended therapy</b>	SABA PRN	Low-dose ICS	Medium-dose ICS or Low-dose ICS + LTRA or Low-dose ICS + LABA* *only if already prescribed by PCP or pulmonologist	Previous medications plus Subspecialist referral

**RESPIRATORY ASSESSMENT AND MANAGEMENT PROTOCOL (RAMP) for Asthma Patients**  
 Patients ≥2 years of age with asthma/wheezing excluding other chronic lung disease, bronchiolitis, bacterial pneumonia, neurological disorders, immunodeficiency diseases, and cardiac patients



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## Appendix A. Asthma Action Plan

## MY HOSPITAL ASTHMA ACTION PLAN - 6/24/2014 for Test Review

- MY ASTHMA LEVEL OF SEVERITY IS: Mild Persistent
- MY ASTHMA TRIGGERS ARE: smoke, air pollution, colds/respiratory infections, mold. Avoid these when possible.
- REMEMBER: WASH MY HANDS and get a YEARLY FLU SHOT to help avoid infections.
- REMEMBER: Use spacer with metered dose inhalers. Rinse mouth after using inhaled controller.

<b>Green Zone Plan</b>	<b>GREEN ZONE MEDICATIONS</b>	
 <p><b>In the Green Zone I have:</b></p> <ul style="list-style-type: none"> <li>• No cough</li> <li>• No wheeze</li> <li>• No chest tightness</li> </ul>	<p><b>My CONTROLLER MEDICINE(S) I should take EVERY DAY to help me stay well:</b> {CONTROLLER MEDS:24665}</p>	
<b>Yellow Zone Plan</b>	<b>YELLOW ZONE MEDICATIONS</b>	
 <p><b>In the Yellow Zone I have:</b></p> <ul style="list-style-type: none"> <li>• Early asthma symptoms</li> <li>• A slight cough or wheeze</li> <li>• The start of a cold</li> </ul>	<p><b>Take QUICK RELIEF Medicine:</b> {YELLOW ZONE MEDS:23512::"Albuterol (Proventil, Ventolin, ProAir) or Xopenex inhaler 4 inhalations every 4 hours as needed with spacer"} Continue taking my <b>GREEN ZONE</b> controller medicine(s)</p> <p><b>CALL MY DOCTOR</b> if I don't get to the <b>GREEN ZONE</b> after <b>24 hours</b>.</p>	
<b>Red Zone Plan</b>	<b>RED ZONE MEDICATIONS</b>	
 <p><b>In the Red Zone I have:</b></p> <ul style="list-style-type: none"> <li>• An increasing cough</li> <li>• Continued or increasing wheeze</li> <li>• Fast breathing</li> </ul>	<p><b>TAKE NOW QUICK RELIEF medicine in YELLOW ZONE or increase to:</b> {RED ZONE MEDS:26557::"Albuterol (Proventil, Ventolin, ProAir) or Xopenex inhaler 6 inhalations every 2-3 hours as needed with spacer for 9-12 hours"} {RED ZONE STEROIDS:26558} Continue taking my <b>GREEN ZONE</b> controller medicine(s)</p> <p><b>CALL MY DOCTOR NOW. Go to the HOSPITAL</b> if I cannot reach my doctor.</p>	
<p><b>DANGER ZONE</b></p>  <p><b>I NEED IMMEDIATE HELP</b></p> <p><b>CALL 911 or go to nearest Emergency Room if:</b></p>	<ul style="list-style-type: none"> <li>- Breathing very hard or fast</li> <li>- Breathing so hard I can't walk or talk</li> <li>- Using neck or stomach muscles to breath</li> <li>- Chest is sucking in between ribs</li> <li>- QUICK RELIEF medications are NOT WORKING</li> <li>- Lips or fingertips look blue</li> <li>- Nose opens wide with breathing.</li> </ul> <p><b>CONTINUE QUICK RELIEF medicine in RED ZONE</b></p>	

My Doctor is: { :19399 } Phone Number: { :19400 } I should follow-up: {Time; follow-up:23707::"within 1 week"}. Completed by: MD INTEGRATED DUAL TCH, MD on 6/24/2014 at 12:47 PM.

**Appendix B. Recommendations for Children <2 Years** <sup>(3)</sup>

The assessment of acute asthma exacerbations in children <2 years can be difficult. The differential diagnosis of symptoms includes aspiration pneumonitis, pneumonia, bronchiolitis, tracheomalacia, and complications of underlying conditions such as congenital anomalies and cystic fibrosis. These children may not respond to the treatment recommendations made in this guideline.

### Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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### Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
  - PICO questions established
  - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
  - British Guideline on the Management of Asthma (2011 and 2016 update), GINA Global Strategy for Asthma Management and Prevention (2012 and 2018 update), NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (2007), and guidelines/pathways from Seattle Children's Hospital (2015) and Children's Hospital of Philadelphia (2017/2018)
3. Literature Review of Relevant Evidence
  - Searched: PubMed, Cochrane, CINAHL, Google Scholar, ProQuest, SumSearch
4. Critically Analyze the Evidence
  - 13 systematic reviews/meta-analyses, 33 randomized controlled trials, and 58 nonrandomized studies
5. Summarize the Evidence
  - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in an

Acute Asthma Exacerbations evidence-based review manual within EBOC.

### Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

**"Evidence Supports"** provides evidence to support an intervention

**"Evidence Against"** provides evidence against an intervention.

**"Evidence Lacking/Inconclusive"** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<b>Recommendation</b>	
<b>STRONG</b>	Desirable effects clearly outweigh undesirable effects or vice versa
<b>WEAK</b>	Desirable effects closely balanced with undesirable effects
<b>Quality</b>	<b>Type of Evidence</b>
<b>High</b>	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
<b>Moderate</b>	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
<b>Low</b>	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
<b>Very Low</b>	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

### Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management of acute asthma exacerbations in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

### Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

### Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

**Version History**

<b>Date</b>	<b>Comments</b>
Nov 2009	Originally completed
Jan 2014	Updated
Jan 2017	Revised
Jan 2019	Updated recommendations on steroids, revised verbiage for referrals, and added recommendation on magnesium dosing. Revised RAMP to reflect a 'maximum' wean of q4h albuterol dosing versus PRN albuterol dosing. Reaffirmed all other practice recommendations.