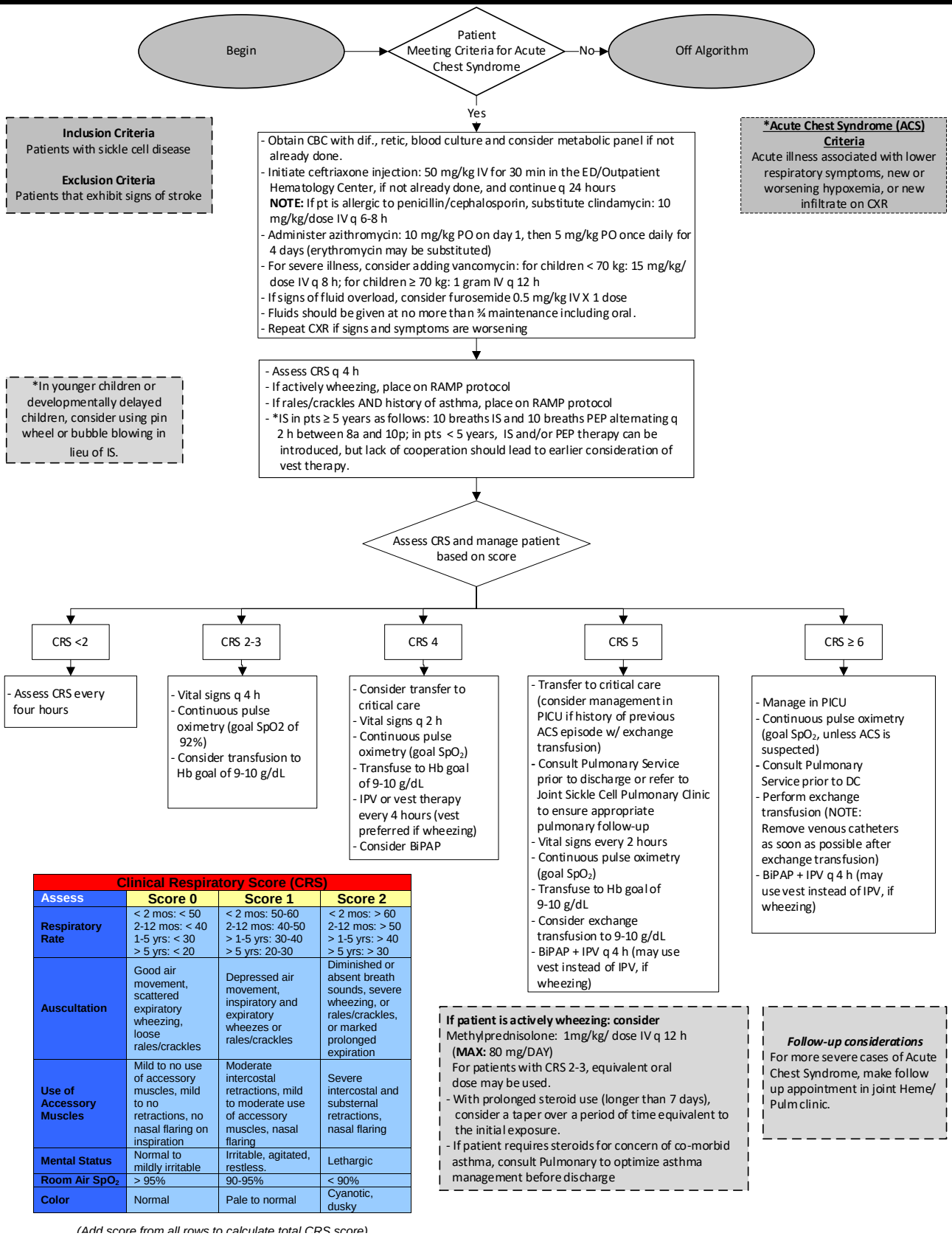
TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Sickle Cell Disease And Acute Chest Syndrome
Evidence-Informed Pathway



Clinical Respiratory Score (CRS)			
Assess	**Score 0**	**Score 1**	**Score 2**
Respiratory Rate	< 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
Auscultation	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
Use of Accessory Muscles	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
Mental Status	Normal to mildly irritable	Irritable, agitated, restless.	Lethargic
Room Air SpO_2	> 95%	90-95%	< 90%
Color	Normal	Pale to normal	Cyanotic, dusky

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

If patient is actively wheezing: consider
Methylprednisolone: 1mg/kg/ dose IV q 12 h
(**MAX:** 80 mg/DAY)
For patients with CRS 2-3, equivalent oral dose may be used.
- With prolonged steroid use (longer than 7 days), consider a taper over a period of time equivalent to the initial exposure.
- If patient requires steroids for concern of co-morbid asthma, consult Pulmonary to optimize asthma management before discharge

Follow-up considerations
For more severe cases of Acute Chest Syndrome, make follow up appointment in joint Heme/Pulm clinic.

Critical Points of Evidence*

Evidence Supports

- Obtain a chest radiograph if patient has cough, chest pain, hypoxemia, or lower respiratory symptoms at presentation to the hospital or during admission. Fever in the absence of these symptoms does not necessitate evaluation with a chest radiograph. [1-6] - Strong recommendation with very low quality evidence
- Encourage oral fluid intake and to administer total fluid intake (intravenous plus oral) at maintenance rate to encourage that the patient remains euvolemic. [7-9] - Strong recommendation with very low quality evidence
  Remarks: Utilize ¾ maintenance fluid if the patient is suspected or confirmed to have acute chest syndrome.
- Use continuous pulse oximetry monitoring in patients with sickle cell disease with fever who are being treated in the emergency center. [10-17] - Strong recommendation with very low quality evidence
- Administer a one week course of prednisolone or three days of dexamethasone to patients who have clinical wheezing with or without a known history of asthma who are being treated in the inpatient setting. [18-22] - Strong recommendation with very low quality evidence
  Remarks: The evidence suggests that corticosteroid use in patients without a history of asthma or other clinical wheezing could present the risk of readmission for rebound pain crisis.
- Encourage incentive spirometry (IS) in patients with sickle cell disease at risk for or with acute chest syndrome who are admitted to the hospital. [6,23-26] - Strong recommendation with low quality evidence
- Administer inhaled bronchodilators every six to eight hours with acute illness if patient has a history of asthma or presents with wheezing. [6,23-26] - Strong recommendation with very low quality evidence
- Transfuse the patient with acute chest syndrome with PRBCs to a hemoglobin goal of 9-10 g/dL. [6,27,28] - Strong recommendation with very low quality evidence

Evidence Against

- Avoid corticosteroids unless indicated. [18-22] – Strong Recommendation with Very Low Quality Evidence

Evidence Lacking/Inconclusive

- Intrapulmonary percussive ventilation (IPV) or vest therapy may be appropriate in the setting of respiratory viral infection with bronchitis or bronchiolitis or for worsening clinical condition when other therapies have not been effective. – Consensus recommendation
- Consider the use of high flow nasal cannula for patients with sickle cell disease and acute chest syndrome when there is increased work of breathing or hypoxemia not responsive to traditional levels of oxygen delivered via a nasal cannula. Please refer the High Flow Nasal Cannula clinical standard for information on this intervention. – Consensus recommendation

Recommendations Adopted/Adapted from National Guidelines

- Obtain a CBC with differential, reticulocyte count and blood culture for all children with fever and sickle cell disease. Consider comprehensive metabolic panel if clinically indicated. [29]
  Remarks: Hemoglobin and retic count should be interpreted relative to baseline values
  - Anemia + low retic = concern for aplastic crisis
  - Anemia + low platelet count + normal retic = concern for splenic sequestration

  Anemia can progress extremely quickly due to low baseline hemoglobin and short half-life of RBCs due to clearance of abnormal cells. This recommendation was adapted from the American College of Emergency Physicians Guideline.
- Promptly administer empiric ceftriaxone for children with SCD and fever. Treat children with SCD who have ACS with intravenous ceftriaxone and oral azithromycin. [6]
  Remarks: This recommendation was adapted from the National Institutes of Health Guideline.
- In patients with SCD, perform urgent exchange transfusion—with consultation from hematology, critical care, and/or apheresis specialists—when there is rapid progression of ACS as manifested by oxygen saturation below 90 percent despite supplemental oxygen, increasing respiratory distress, progressive pulmonary infiltrates, and/or decline in hemoglobin concentration despite simple transfusion.
  Remarks: A CRS score ≥6 represents increasing respiratory distress. This recommendation was adapted from the National Institutes of Health Guideline. [6,30-32]

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

Antibiotics		
Medication	**Dosing**	**Indication/Notes**
Ceftriaxone	Ceftriaxone 50 mg/kg IV every 24 hours	
Azithromycin	Azithromycin 10 mg/kg PO on day 1 (**MAX**: 500 mg/dose), then 5 mg/kg PO once daily (**MAX**: 250 mg/dose) for 4 days (erythromycin may be substituted)	Antimicrobial – Inpatient / Atypical Coverage
Additional Medications Based Upon Patient Condition		
Vancomycin	Children < 70 kg: 15 mg/kg/dose IV q 8 h; for Children ≥ 70 kg: 1 gram IV q 12 h (**MAX:** 1 gram/dose)	For severe illness only, consider adding vancomycin

Measures

Process

- Documentation of CRS scores every 4 hours
- Incidence of pulmonary treatments
- Length of time on oxygen
- Frequency of ambulation
- Percent of patients with CRS ≥5 referred to pulmonary clinic
- Percent of patients/caregivers who received IS and IS education
- CRS score of patients transferred to critical care

Outcome

- Number of patients who develop ACS
- Number of simple blood transfusions
- Number of exchange transfusions
- Number of patients transferred to critical care
- ED and IP LOS
- Number of patients with ACS with identified pathogen

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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.

Sickle Cell Disease With Fever and Acute Chest Syndrome Content Expert Team

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No relevant financial or intellectual conflicts to report.

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
   - National Institute of Health, Evidence-Based Management of Sickle Cell Disease Expert Panel Report, 2014; National Institute for Health Care Excellence (NICE), Sickle Cell Disease: Managing Acute Painful Episodes in Hospital, 2012; American College of Emergency Physicians, Sickle Cell – Point of Care Tools, 2023; American Society of Hematology, Sickle Cell Disease: Transfusion Support Pocket Guide for the Children, 2020; British Society of Haematology, Guidelines on Red Blood Cell Transfusion in Sickle Cell Disease Part II: Indications for Transfusion, 2016; British Society of Haematology, Guideline on the Management of Acute Chest Syndrome in Sickle Cell Disease, 2016
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane Collaboration
4. Critically Analyze the Evidence
   - Four randomized **controlled** trials, and twenty-two nonrandomized studies, as applicable
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in an electronic database.

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.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	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
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	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 diagnosis/management of sickle cell disease with fever and acute chest syndrome 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

Date	Comments
2/2024	Originally Completed