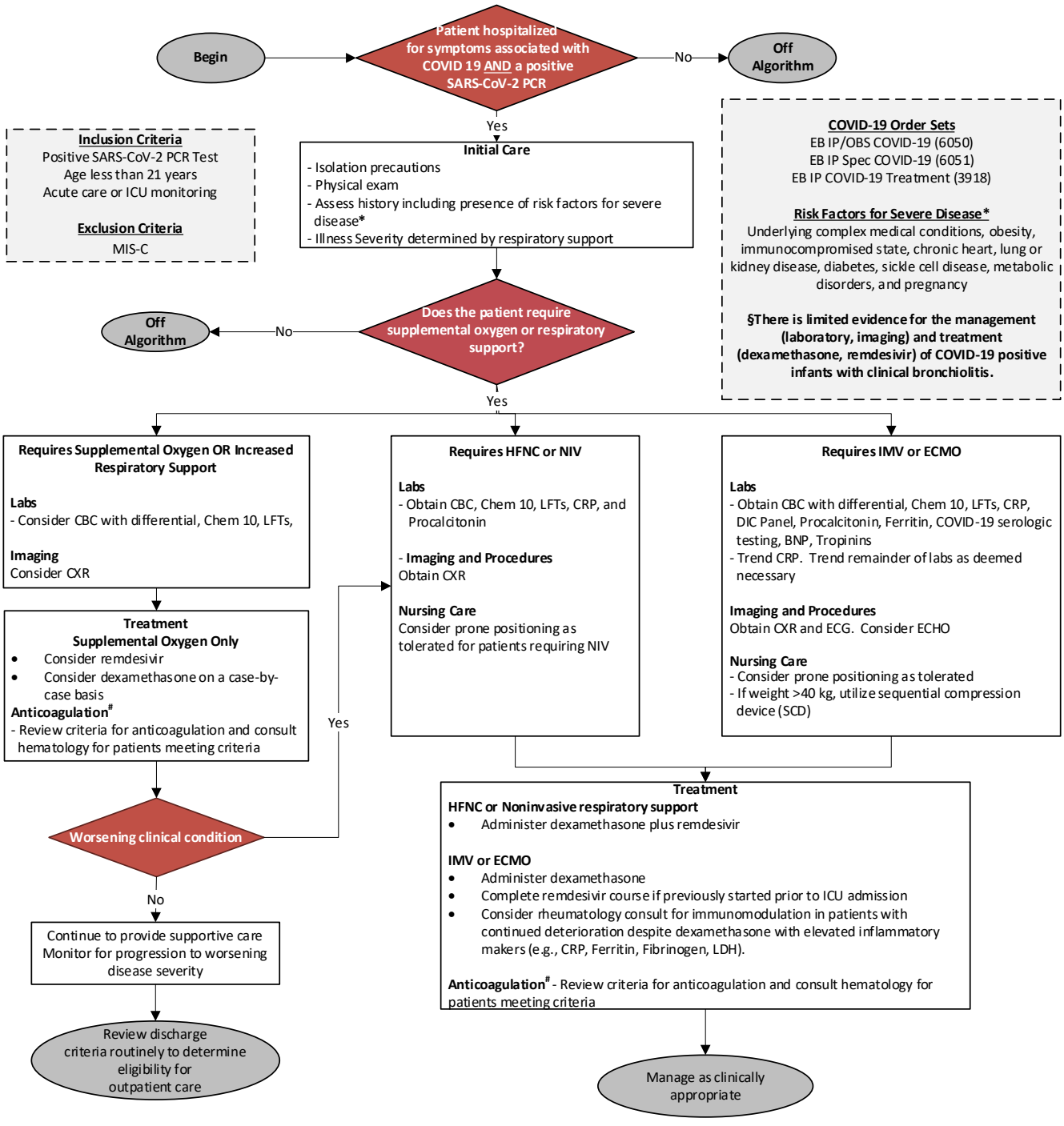
Texas Children's Hospital

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Care of the Hospitalized Patient with COVID-19
Evidence-Informed Pathway



Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

Critical Points of Evidence*

Evidence Supports

Dexamethasone

- Low-dose dexamethasone should be administered to pediatric patients with positive SARS-CoV-2 RT-PCR requiring high flow nasal cannula, in hospitalized patients with progressive disease requiring increasing respiratory support, and in hospitalized patients who require positive pressure or mechanical ventilation. [1-16] - Strong recommendation, low quality evidence
  Remarks: Dexamethasone should be dosed at 0.15 mg/kg/dose (MAX 6mg) once daily for 10 days (or until discharge) unless there is another indication for continuing treatment. Dexamethasone may be discontinued prior to 10 days for patients with rapid improvement and no longer requiring supplemental oxygen. Dexamethasone plus remdesivir should be considered in patients with progressive respiratory disease requiring increasing respiratory support and patients with severe disease.

Remdesivir

- Consider the use of remdesivir in hospitalized pediatric patients with positive SARS-CoV-2 RT-PCR test result requiring supplemental oxygen or an increase in baseline respiratory support, and in hospitalized patients with progressive disease requiring increasing respiratory support. [15-32] – Weak recommendation, moderate quality evidence
  Remarks: Evidence suggests that treatment with remdesivir is most beneficial early in the course of illness. The benefit in critically ill patients is less clear. We recommend starting remdesivir as a 5-day course or until hospital discharge.

Immunomodulators

- Consider rheumatology consult for immunomodulation in patients with continued deterioration and elevated inflammatory markers (e.g., CRP, Ferritin, Fibrinogen, LDH) despite administration of dexamethasone.[15,16,33-40] – Weak recommendation, moderate quality evidence

Recommendations Adopted from Other Guidelines

Anticoagulation

- Prophylactic anticoagulation should be administered for all hospitalized patients ≥18 years of age who have been diagnosed with primary COVID-19. – Adopted from COVID-19 and Thromboembolism Prophylaxis: Recommendations in Children, Adolescents and Young Adults TXCH Supportive Care Practice Standard [41]
- Consider prophylactic anticoagulation for hospitalized patients <18 years of age diagnosed with primary COVID-19 in the following scenarios after consultation with the Hematology team. – Adopted from COVID-19 and Thromboembolism Prophylaxis: Recommendations in Children, Adolescents and Young Adults TXCH Supportive Care Practice Standard [41]
  - Any patient admitted to the intensive care unit and requiring critical care monitoring
    OR
  - Any patient ≥12 years of age **AND** with one or more risk factors for COVID-19 associated thromboembolism. Risk factors include active cancer, sickle cell disease, presence of central line, personal history of thrombosis, inherited thrombophilia, and obesity [BMI >95th percentile of age).

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

Measures

Process

- Length of Stay (Inpatient, ICU)

Outcome

- Mortality Rate
- Ventilation Days
- Rate of Acute Respiratory Distress Syndrome
- Days on ECMO support
- Rate of Thrombotic Events
- Rate of Cardiac Complications

Dosing for Treatment and Adjunctive Therapy [29,58]

Medication	Dose	Additional Details
Dexamethasone	**Children and Adolescents <40 kg:** • 0.15 mg/kg/dose (**MAX** 6mg) once daily for 10 days (or until discharge) **Children and Adolescents ≥40 kg:** • 6mg once daily for 10 days (or until discharge)	• Equivalent steroid may be indicated for pregnant women based upon gestational age • Contact pharmacy for equivalent steroid
Remdesivir	**Infants and Children ≥ 28 days old and <12 years:** • 3 kg to <40 kg: IV: Loading dose: 5 mg/kg/dose on day 1, followed by 2.5 mg/kg/dose once daily • ≥40 kg: IV: Loading dose: 200 mg on day 1, followed by 100 mg once daily **Children ≥12 years and Adolescents:** • <40 kg: IV: Loading dose: 5 mg/kg/dose on day 1, followed by 2.5 mg/kg/dose once daily • ≥40 kg: IV: Loading dose: 200 mg on day 1, followed by 100 mg once daily	• Monitor at baseline and trend liver function tests (LFTs), partial thromboplastin time (PTT), renal function tests, and signs/symptoms of infusion reaction. • Consider discontinuation with elevation of LFTs or signs/symptoms of liver inflammation.
Anticoagulation	Review the COVID-19 and Thromboembolism Prophylaxis: Recommendations in Children, Adolescents and Young Adults TXCH Supportive Care Practice Standard for details on dosing	

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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.

Care of the Hospitalized Patient with COVID-19 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 Institutes of Health, COVID-19 Treatment Guidelines, 2021; Infectious Disease Society of America, Guidelines on the Treatment and Management of Patients with COVID-19, 2021; American College of Physicians, Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid Living Practice Points From the American College of Physicians (Version 2, Update Alert 3), 2022
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane
4. Critically Analyze the Evidence
   - 60 meta-analyses, 12 randomized **controlled** trials, and 2 nonrandomized studies, and 7 guidelines
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Care of the Hospitalized Patient with COVID-19 evidence-based review electronic file 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.

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 management of COVID-19 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 should 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.

Permission of Use

Version History

Date	Comments
May 2021	Originally Completed
Sept 2021	Revised
Nov 2021	Revised
Dec 2021	Revised – Added high titer to the algorithm wording for convalescent plasma
May 2022	Revised – Changed dosing eligibility for Remdesivir. Removed links for the Remdesivir EUA and fact sheet.
Sept 2022	Dexamethasone and Remdesivir recommendations revised; Post-Exposure Prophylaxis content removed
May 2026	Updated; Format Changed to Pathway