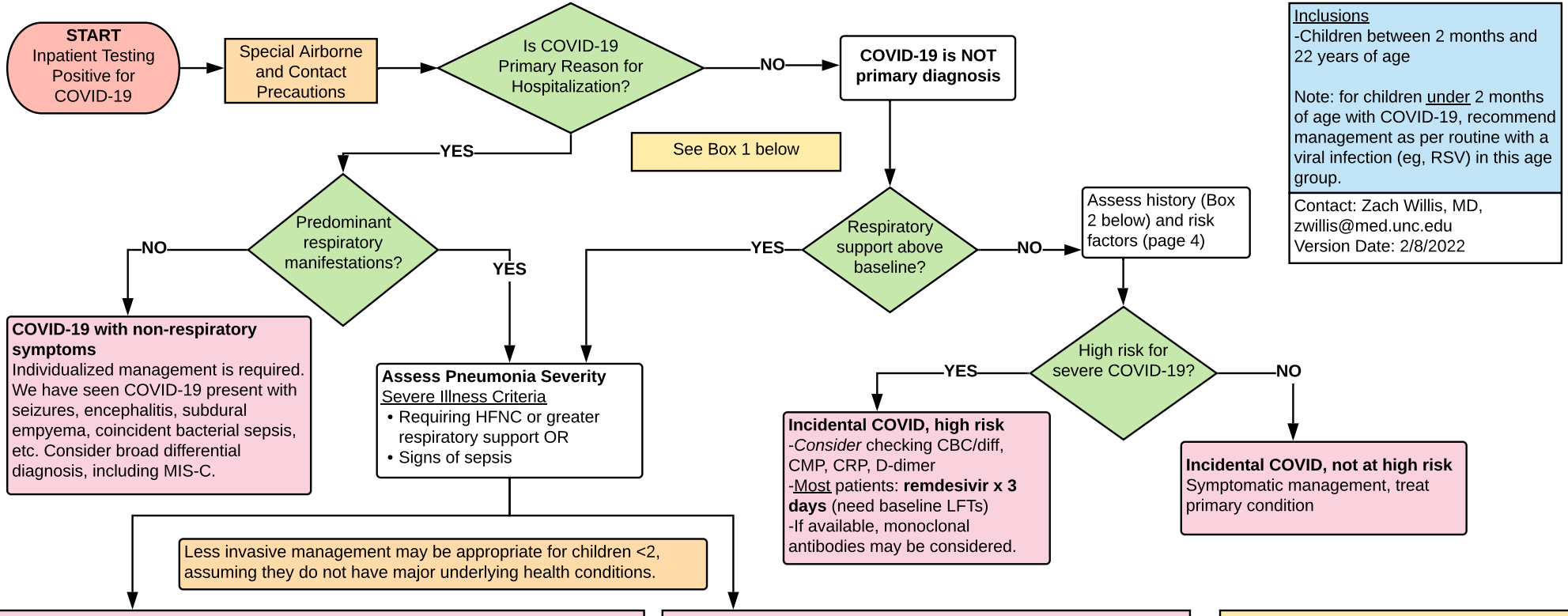
UNC Children's COVID-19 Guidelines

Page 1: Acute COVID-19 Inpatient Algorithm



Inclusions
-Children between 2 months and 22 years of age

Note: for children under 2 months of age with COVID-19, recommend management as per routine with a viral infection (eg, RSV) in this age group.

Contact: Zach Willis, MD, zwillis@med.unc.edu
Version Date: 2/8/2022

Severe COVID-19

	Age ≥12	Age 2-12, wt >3.5 kg	Age <2, >3.5 kg
Disposition	ICU or Intermediate	ICU or intermediate	ICU or intermediate
Labs	CBC/diff, CMP, LDH, CRP, ESR, DIC panel, troponin I, BNP, EKG	CBC/diff, CMP, LDH, CRP, ESR, DIC panel, troponin I, BNP, EKG	Consider CBC/diff, CMP, CRP
Imaging	CXR	CXR	CXR
As-needed evaluations	CTA chest, echo, neuroimaging, PVLs	CTA chest, echo, neuroimaging, PVLs	Severe COVID labs, echo
Recommended Consults	Pulmonary, ID, Hematology	Pulmonary, ID	If HFNC: none; if intubated: Pulm, ID
As-needed Consults	Cardiology	Hematology, Cardiology	Pulm, ID, Hem, Cardiology
Treatment (usual)	Remdesivir plus dexamethasone	Remdesivir plus dexamethasone	Usually remdesivir
Anticoagulation (refer to p3)	Most patients	Some patients	Rarely indicated
Rapid worsening with CRP >75	Consider addition of baricitinib OR tocilizumab	May sometimes consider baricitinib OR tocilizumab	Consider dexamethasone

COVID-19 Without Severe Signs

	Age ≥12	Age 2-12	Age <2, >3.5 kg
Disposition	Floor	Floor	Floor
Labs	CBC/diff, CMP, CRP, DIC Panel	CBC/diff, CMP, CRP	Consider CBC/diff, CMP, CRP
Imaging	CXR	CXR	CXR
As-needed evaluations	Severe COVID labs	Severe COVID labs	Severe COVID labs
Recommended Consults	None	None	None
As-needed Consults	Pulmonary, ID, Hematology	Pulmonary, ID, Hematology	Pulmonary, ID, Hematology
Treatment (usual)	Remdesivir	Remdesivir	May consider remdesivir
Anticoagulation (refer to p3)	Most patients	Some patients	Rarely indicated
Progressive worsening	Consider dexamethasone	Consider dexamethasone	Consider dexamethasone

Box 1: Is COVID-19 Primary Diagnosis?

Patients admitted for another condition may be incidentally positive for COVID-19.

Useful questions:
-Was this admission scheduled?
-Was the patient already in the hospital?
-Was respiratory infection suspected before COVID-19 test was sent?
-Is there evidence of pneumonia?

Box 2: Key Historical Details

- Symptom onset date
- Vaccination status
- Household contacts with COVID-19, including timing
- History of respiratory disease (asthma, pneumonia, sleep apnea, etc.)
- History of liver or kidney disease

UNC Children's COVID-19 Guidelines
Page 2: Treatments used for Acute COVID-19

Agent	Dosing and Regimen	Considerations	Adverse Effects and Interactions	Recommendation
Frequently Used in Hospitalized Pediatric Patients with Acute COVID-19				
Remdesivir FDA approved for patients ≥12 years and ≥40 kg. Other patients: available under EUA.	<40 kg: 5 mg/kg IV x1, then 2.5 mg/kg IV daily ≥40 kg: 200mg IV x1, then 100mg IV daily Treatment course: 5 days Prevention of progression: 3 days	Criteria (abbreviated): SpO2 <94% on RA. eGFR > 30. ALT < 5x ULN. Hospitalized <10 days; intubated <5 days. Not pregnant.	Nausea, vomiting, elevation of hepatic transaminases. Bradycardia has been reported. Check LFTs at baseline and as PRN; do not start or stop if ALT is >5x ULN. Generally avoided if eGFR <30.	**Recommended** in patients admitted for COVID-19 and requiring supplemental oxygen or greater support. **Consider** in patients considered at high risk to progress to requiring respiratory support.
Dexamethasone	<40 kg: 0.15 mg/kg PO/IV daily >40 kg: 6 mg PO/IV daily Alternatives: prednisolone 1 mg/kg daily (40 mg max), methylpred 0.8 mg/kg daily (32 mg max)	Proven benefit for *adults* requiring oxygen or greater respiratory support. Other corticosteroids would likely have similar effect.	Hypertension +/- PRES, bradycardia, delirium	**Consider** if requiring low-flow oxygen, especially if consistent or escalating requirement. **Recommended** if requiring HFNC or greater respiratory support.
Heparin OR **Low molecular-weight heparin**	See Page 3 for anticoagulation recommendations.			**Used in most cases of COVID-19.** See page 5 for detailed recommendations.
Rarely used in Pediatric Patients with Acute COVID-19				
Tocilizumab *Recommend Rheumatology consultation first*	8 mg/kg/dose x1, max 800 mg Monoclonal antibody against IL-6	In adult patients, recommended if receiving HFNC or greater support, or if worsening and high CRP (>75).	Avoid if: already immune suppressed, neutropenic, platelets <50K, ALT >5x ULN, concern for pre-existing chronic infection such as TB or *Strongyloides*	**Consider only in critical COVID-19**. Not generally recommended. Used in addition to other therapies (steroids, remdesivir, etc.).
Baricitinib Available under EUA for acute COVID-19 down to age 2 *Recommend Rheumatology consultation first*	≥9 years: 4 mg PO daily <9 years: 2 mg PO daily Can be dispersed in water and taken PO or via NG or GT	JAK inhibitor used as anti-inflammatory. Similar criteria as for tocilizumab.	Thrombosis is more common; patients must be on thromboprophylaxis unless contraindicated.	**Not generally recommended.** May be considered as alternative to tocilizumab when toci unavailable or contraindicated. **Do not co-administer with tocilizumab.**
Used ONLY for Outpatients (or inpatients admitted for another reason)				
Monoclonal Antibodies Casirivimab/imdevimab Bamlanivimab/etesevimab Sotrovimab	Cas/Imd: 600/600 mg IV x1 Bam/Ete: 700/1400 mg IV x1 Sotrovimab: 500 mg IV x1 As of this writing, **Sotrovimab** is the only available product due to efficacy against Omicron variant	Monoclonal antibodies against the spike protein. 1-2-hour infusion with at least 1 hour observation. No benefit in patients hospitalized for COVID-19.	Infusion reactions (fever, chills, hypotension) may occur. Anaphylaxis may rarely occur.	**Rarely recommended inpatient.** Occasionally may be used in patients *admitted for another reason* and found to have COVID-19 and meeting criteria for treatment. Depending on supply.

UNC Children's COVID-19 Guidelines

Page 3: Anticoagulation Management in Pediatric COVID-19

START
Patient admitted with acute COVID-19 AND
- 12 years or older OR
- 2 years or older with severe COVID-19 (see p1)

Initial Labs
CBC/diff, retic, CMP, DIC panel, FVIII, AT3, ferritin, LDH

Determine Thrombosis Risk Group

Group A: Therapeutic Anticoagulation
Any of the following:
- Confirmed DVT/PE or other indication for therapeutic anticoagulation
- High suspicion of DVT/PE but not documented. Strongly consider if O2 requirement if >5L HFNC
- Hemodialysis with repetitive clotting of dialysis tubing
- MIS-C with coronary artery aneurysm and Z-score >=10
- MIS-C with documented VTE *or* ejection fraction (EF) < 35%

Group B: Prophylactic Anticoagulation
- Hospitalized patients ≥12 years: follow "Pediatric VTE Prophylaxis" order set
- Hospitalized patients <12 years: consider Pediatric VTE Prophylaxis if altered mobility and ≥ 2 VTE risk factors (Table 1)
- **Consider** Pediatric Hematology consult if initial D-dimer >10x ULN (>2,500 ng/mL) or rising

Daily Labs
CBC/diff, DIC Panel (consider less frequent if stable)

Treat with
Enoxaparin (target anti-Xa level 0.6-1; monitor renal function)
or
UFH (Heparin Pediatric Nomogram: Thrombosis Panel, target hep correlation or anti-Xa: 0.3-0.7 U/ml). Consider heparin for first 48 hours if clinically unstable
UNC Medical Center: Heparin Guideline

Prophylaxis with
Enoxaparin (monitor renal function)
or
UFH (Heparin Pediatric Nomogram: Sub-Therapeutic Panel)

*Order via Peds VTE PPX order set
UNC Health:VTE Prophylaxis Guideline

Table 1. Risk Factors for Hospital-Associated VTE in Children

- Central venous catheter
- Mechanical ventilation
- Prolonged length of stay (eg, anticipated >3 days)
- Complete immobility (eg, Braden Q Mobility Score = 1)
- Obesity (BMI > 95th percentile)
- Active malignancy, nephrotic syndrome, CF exacerbation, sickle cell disease vaso-occlusive crisis, or flare of underlying inflammatory disease (eg, lupus, JIA, IBD)
- Congenital or acquired heart disease with venous stasis or impaired venous return
- Previous history of VTE
- First-degree family history of VTE before age 40 or unprovoked VTE
- Known thrombophilia (eg Protein S, Protein C, or anti-thrombin deficiency; Factor V Leiden; factor II G0210A; persistent antiphospholipid antibodies
- Pubertal, post-pubertal, or age > 12 years
- Estrogen-containing oral contraceptive pill
- Status-post splenectomy for underlying hemoglobinopathy

Table 2. Management After Hospital Discharge

Continued anticoagulant thromboprophylaxis post-discharge from hospital can be *considered* in patients with COVID-19 or MIS-C who have markedly elevated D-dimer levels at discharge and superimposed clinical risk factors for VTE with a planned duration of the sooner of clinical risk factor resolution or 30d post discharge
- Patients with MIS-C and documented thrombosis or an Ef <35% should receive therapeutic anticoagulation with enoxaparin until at least two weeks after discharge from the hospital
  - Indications for longer outpatient therapeutic enoxaparin dosing include: CAA with z-score >10 (indefinite treatment), documented thrombosis (treatment ≥ 3mos pending thrombus resolution), or ongoing moderate to severe left ventricular dysfunction
- Any patient with COVID-19 discharged from the hospital should be educated about the 4 main symptoms of DVT (swelling, pain, redness, warmth), PE (SOB, CP, tachycardia, cough/hemoptysis), CSVT (worsening headache, nausea/vomiting, changes in vision, or focal neuro deficits). www.clotconnect.org
- Anticoagulation of choice: enoxaparin if <15 yo or apixaban if >15 yo AND weight of>50 kg.
- Patients on anticoagulation should have a pediatric hematology consultation AND follow up within 2 weeks of discharge.

UNC Children's COVID-19 Guidelines
Page 4: Risk Factors for Severe Disease

Patients with these risk factors are probably more likely to develop complications or severe disease. Data is limited. Other patients not fitting in these categories may also be at increased risk and should be considered on a case-by-case basis.

Putative Risk Factors	Comments
Immunocompromised Status Hematopoietic stem cell transplant recipient Solid organ transplant recipient Receiving anticancer chemotherapy Primary immunodeficiency HIV infection Chronic steroid therapy Other immunosuppressive medications (e.g., TNF blockade)	Few immunocompromised children in our hospital have had severe pneumonia but some have had prolonged course. Some, especially on high-dose steroids, have had significant pneumonia.
Hematologic Disease Sickle-cell disease	Limited data, but patients likely at increased risk for severe pneumonia.
Symptomatic cardiac disease Major congenital heart defects Cardiomyopathy	Limited data. Caution and careful follow-up are advised
Significant pulmonary disease Severe chronic lung disease with lung function <50% or ≥2 hospitalizations in the past year Oxygen while awake and/or asleep Tracheostomy Pulmonary hypertension Asthma requiring daily controller Obstructive sleep apnea	Baseline compromised pulmonary function likely increases the risk of requiring hospitalization and risk of severe disease. **Many hospitalized patients have had baseline OSA or poorly controlled asthma.**
Metabolic, renal, and endocrine disease Diabetes mellitus requiring insulin Obesity (BMI >95th percentile or >30), **especially BMI >99th percentile or >35** Metabolic disorders significantly affecting multiple organ systems Chronic kidney disease, especially renal replacement therapy	These are clear risk factors in adults. **Most adolescents with severe COVID-19 in our hospital have been obese.**
Medically complex Technology dependence associated with developmental delay and/or genetic abnormalities	These patients have diminished tolerance for an acute infection.

UNC Children's COVID-19 Guidelines
Page 5: Post-discharge Follow-up Recommendations

These are guidelines only. Follow-up plans must be individualized for each patient.

	Acute COVID-19
Acute COVID-19 service	Contact PCP at discharge
Primary care physician	Consider check-in 3-5 days after discharge. Phone or virtual generally OK.
Pulmonology	*If admitted *for* symptomatic COVID-19* -1-month symptom check (virtual OK) -2-month in-person: PFTs and 6-minute walk test
Hematology	If discharged on anticoagulation, virtual follow-up within 2 weeks.
Rheumatology	If discharged on immunomodulator (e.g., prednisone, anakinra), follow-up within 2 weeks. Virtual OK.
Cardiology	As needed only
Infectious Diseases	As needed only

Special Precautions during follow-up:
Most patients recovering from acute COVID-19 are considered to have cleared within 10 days of symptom onset (most) or 21 days (if severe disease or immunocompromised). MIS-C patients are almost always fully recovered from acute COVID-19. For patients meeting those time-based criteria, clinics should use routine, per-policy approach.