Clinical Management of Children Summary

Last Updated: February 29, 2024

Data from the Centers for Disease Control and Prevention demonstrate that severe disease and death due to COVID-19 occur less often in children than in adults.[1-4] However, weekly hospitalization rates for children aged <6 months are high, exceeded only by the rates for adults aged ≥75 years.[5] The overall incidence of SARS-CoV-2 infection and, by extension, COVID-19–related hospitalizations among children increased substantially with the emergence of newer variants, particularly the Omicron variant and its subvariants.[6,7] According to the Centers for Disease Control and Prevention, by December 2022, an estimated 96% of children and adolescents had serologic evidence of prior SARS-CoV-2 infection.[8] The high infection rates among children makes the overall burden substantial despite the low rate of severe outcomes.[9]

Data on the pathogenesis and clinical spectrum of SARS-CoV-2 infection in children are still limited compared to the data for adults. Although only a small percentage of children with COVID-19 will require medical attention, the percentage of intensive care unit admissions among hospitalized children is comparable to that for hospitalized adults with COVID-19.[6,10-18]

Observational studies and meta-analyses have found that children with certain comorbidities are at increased risk of severe COVID-19. These comorbidities include cardiac disease, neurologic disorders, prematurity (in young infants), diabetes, obesity (particularly severe obesity), chronic lung disease, feeding tube dependence, and immunocompromised status.[19-22] Demographic factors, such as age (<1 year and 10–14 years)[23] and non-White race/ethnicity,[15,24-26] have also been associated with severe disease. However, many studies did not assess the relative severity of underlying medical conditions in children with severe COVID-19.

In general, COVID-19 has similar clinical manifestations and disease stages in children and adults, including an early phase driven by viral replication and a late phase that appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage. Respiratory complications in young children that can occur during the early clinical phase include croup and bronchiolitis. In addition, a small number of children who have recovered from acute SARS-CoV-2 infection develop multisystem inflammatory syndrome in children (MIS-C) 2 to 6 weeks after infection. MIS-C is a postinfectious inflammatory condition that can lead to severe organ dysfunction.

Published guidance on the treatment of COVID-19 in children has been extrapolated mostly from recommendations for adults with COVID-19, recommendations for children with other viral infections, and expert opinion.[27-29] Applying adult data from COVID-19 trials to children is a unique challenge because most children experience a mild course of illness with COVID-19.[30] Relative to adults, children with COVID-19 have substantially lower mortality and less need for hospitalization.[10,11,31] Because of these differences in epidemiology and disease severity, the effect sizes of treatments for children are likely to be smaller than those observed in adults. Therefore, to produce a beneficial outcome in children, the number needed to treat is higher. Collectively, these factors influence the risk versus benefit balance for pharmacologic therapies in children.

In the absence of sufficient clinical trial data on the treatment of children with COVID-19, the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations for the therapeutic management of hospitalized children are based largely on safety and efficacy data from clinical trials in adults, the child's risk of disease progression, and expert opinion.

In general, data from clinical trials in adults are most applicable to the treatment of older children

with severe COVID-19 and predominantly lower respiratory tract disease. Using data from clinical trials in adults to develop recommendations for children with SARS-CoV-2 infection who have clinical syndromes associated with other respiratory viruses (e.g., bronchiolitis, croup, asthma) is a challenge. No evidence suggests that these syndromes should be managed differently when caused by SARS-CoV-2 infection. Clinical judgment is needed when applying recommendations for treatment in adults to children, particularly young children, with these clinical syndromes.

The Panel's recommendations for the management of children with COVID-19 or MIS-C are summarized in the tables below. Table 3a provides recommendations for the therapeutic management of nonhospitalized children with COVID-19. The Panel's recommendations are stratified by age (per the Food and Drug Administration Emergency Use Authorizations) and risk level. See Therapeutic Management of Nonhospitalized Children With COVID-19 for more information. Table 3b includes a framework to help clinicians evaluate the risk for severe COVID-19 based on patient conditions and COVID-19 vaccination status.

The recommendations for hospitalized children in Table 3c are stratified by disease severity. See Therapeutic Management of Hospitalized Children With COVID-19 for more information. Table 3d summarizes the recommendations for the therapeutic management of MIS-C. For the rationale behind these recommendations and supporting data, see Therapeutic Management of Hospitalized Children With MIS-C, Plus a Discussion on MIS-A.

Table 3a. Therapeutic Management of Nonhospitalized Children With COVID-19

Risk of Severe COVID-19	Panel's Recommendations	
	Aged 12–17 Years	Aged <12 Years
Symptomatic, Regardless of Risk Factors	• Provide supportive care **(AIII)**.	• Provide supportive care **(AIII)**.

High Risk[a,b]	• Use 1 of the following options (listed in order of preference):[c]
	  • **Ritonavir-boosted nirmatrelvir (Paxlovid)** within 5 days of symptom onset **(BIII)**
	  • **Remdesivir** within 7 days of symptom onset **(CIII)**
		• Ritonavir-boosted nirmatrelvir is not authorized by the FDA for use in children aged <12 years.
		• There is insufficient evidence to recommend either for or against the routine use of remdesivir. Consider treatment based on age and other risk factors.

Intermediate Risk[b,d]	• There is insufficient evidence to recommend either for or against the use of any antiviral therapy. Consider treatment based on age and other risk factors.	• There is insufficient evidence to recommend either for or against the routine use of remdesivir.
Low Risk[b,e]	• Manage with supportive care alone **(AIII)**.	• Manage with supportive care alone **(AIII)**.
Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.		

[a] Molnupiravir is not authorized by the FDA for use in children aged <18 years and should not be used.

[b] See Table 3b for the Panel's framework for assessing the risk of progression to severe COVID-19 based on patient conditions and COVID-19 vaccination status.

[c] Initiate treatment as soon as possible after symptom onset.

[d] The relative risk of severe COVID-19 for intermediate-risk patients is lower than the risk for high-risk patients but higher than the risk for low-risk patients.

[e] Low-risk patients include those with comorbid conditions that have a weak or unknown association with severe COVID-19.

Patients with no comorbidities are included in this group.

Key: FDA = Food and Drug Administration; the Panel = the COVID-19 Treatment Guidelines Panel

Table 3b. The Panel's Framework for Assessing the Risk of Progression to Severe COVID-19 Based on Patient Conditions and COVID-19 Vaccination Status

Conditions	Risk Level by Vaccination Status	
	Not Up to Date[a,b]	Up to Date[a]
Strong or Consistent Association With Progression to Severe COVID-19		
• Moderately or severely immunocompromised (see Special Considerations in People Who Are Immunocompromised)	High	
• Obesity (BMI ≥95th percentile for age), especially severe obesity (BMI ≥120% of 95th percentile for age)[c] • Medical complexity with dependence on respiratory technology[d] • Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitations in self-care or activities of daily living • Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily • Severe congenital or acquired cardiac disease • Multiple moderate to severe chronic diseases • Pregnancy	High	
Moderate or Inconsistent Association With Progression to Severe COVID-19		
• Aged <1 year • Prematurity in children aged ≤2 years • Sickle cell disease • Diabetes mellitus (poorly controlled) • Chronic kidney disease • Nonsevere cardiac, neurologic, or metabolic disease[e]	Intermediate	
Weak or Unknown Association With Progression to Severe COVID-19		
• Mild asthma • Overweight • Diabetes mellitus (well controlled)	Low	

[a] See the current COVID-19 vaccination schedule from the CDC.

[b] Recent SARS-CoV-2 infection (i.e., within 3–6 months) may confer substantial immunity against closely related variants. A patient's recent infection history should be factored into the risk assessment.

[c] The degree of risk conferred by obesity in younger children is less clear than it is in older adolescents.

[d] This includes patients with a tracheostomy and those who require NIV.

[e] The data for this group are particularly limited.

Key: BMI = body mass index; CDC = Centers for Disease Control and Prevention; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel

Table 3c. Therapeutic Management of Hospitalized Children With COVID-19

Disease Severity	Panel's Recommendations
Hospitalized for COVID-19	For children aged ≥12 years admitted for COVID-19, use prophylactic anticoagulation unless contraindicated **(BIII)**.[a]
Does Not Require Supplemental Oxygen	For children admitted for COVID-19 who are at the highest risk of progression to severe COVID-19[b] (especially those who are severely immunocompromised), consider using **remdesivir**[c] for children aged 12–17 years **(CIII)**. There is insufficient evidence for using remdesivir in children aged 28 days to <12 years and weighing ≥3 kg.
	For children admitted for reasons other than COVID-19 who have mild to moderate COVID-19 and are at the highest risk of progression,[b] refer to Therapeutic Management of Nonhospitalized Children With COVID-19.
Requires Conventional Oxygen[d]	Use 1 of the following options: • **Remdesivir**[c] **(BIII)** • **Dexamethasone plus remdesivir**[c] for children with increasing oxygen needs, particularly adolescents **(BIII)**
Requires Oxygen Through High-Flow Device or NIV[e]	Use 1 of the following options: • **Dexamethasone (BIII)** • **Dexamethasone plus remdesivir**[c] **(BIII)**
	For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, **baricitinib**[f] or **tocilizumab** can be considered for children aged 12–17 years **(BIII)** and for children aged 2–11 years **(CIII)**.
Requires MV or ECMO[g]	**Dexamethasone**[g] **(AIII)**
	For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, **baricitinib**[f] or **tocilizumab** may be considered for children aged 12–17 years **(BIII)** and for children aged 2–11 years **(CIII)**.
Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.	

[a] Weighing the risk factors for thrombosis and bleeding, some Panel members would use prophylactic anticoagulation for children aged <12 years who are hospitalized for COVID-19.

[b] See Therapeutic Management of Nonhospitalized Children With COVID-19 for a list of conditions that will put children at highest risk for progression to severe COVID-19.

[c] The clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset. Remdesivir should be given for 5 days or until hospital discharge, whichever comes first. Examples of patients who may benefit most from adding remdesivir >10 days from symptom onset include patients who are severely immunocompromised, particularly if they have evidence of ongoing viral replication (e.g., those with a low Ct value, as measured by an RT-PCR result or with a positive rapid antigen test result).

[d] Conventional oxygen refers to oxygen supplementation that is not high-flow oxygen, NIV, MV, or ECMO.

[e] Patients who are receiving NIV or MV at baseline and require a substantial increase in baseline support should be treated per the recommendations for patients requiring new NIV or MV.

[f] **Tofacitinib** is an alternative if baricitinib is not available **(BIII)**.

[g] For children who started receiving remdesivir before admission to the ICU, the remdesivir should be continued to complete the treatment course.

Key: ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; MV = mechanical ventilation; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel; RT-PCR = reverse transcription polymerase chain reaction

Table 3d. Therapeutic Management of Hospitalized Patients With MIS-C

	Panel's Recommendations

MIS-C	**Initial treatment for MIS-C includes both immunomodulatory and antithrombotic therapy.**
	Initial Immunomodulatory Therapy
	• IVIG 2 g/kg IBW IV (up to a maximum total dose of 100 g) **plus** low to moderate dose **methylprednisolone** (1–2 mg/kg/day IV)[a] or another glucocorticoid at an equivalent dose[a] **(AIIb)**.
	• **Glucocorticoid monotherapy**, **only** if IVIG is unavailable or contraindicated **(BIIa)**.
	• **IVIG monotherapy**, **only** if glucocorticoids are contraindicated **(BIIb)**.
	Intensification Immunomodulatory Therapy
	• Intensification therapy is recommended for children with refractory MIS-C who do not improve within 24 hours of receiving initial immunomodulatory therapy **(AIII)**. One of the following can be used (listed in alphabetical order):
	  • High-dose **anakinra** 5–10 mg/kg/day IV (preferred) or SUBQ in 1–4 divided doses[b] **(BIIb)**
	  • Higher-dose **glucocorticoid** (e.g., **methylprednisolone** 10–30 mg/kg/day IV for 1–3 days, up to a maximum of 1,000 mg/day, or equivalent glucocorticoid for 1–3 days)[a,b] **(BIIb)**
	  • **Infliximab** 5–10 mg/kg IV for 1 dose[b,c] **(BIIb)**
	Antithrombotic Therapy
	• Low-dose **aspirin** (3–5 mg/kg PO once daily, up to a maximum dose of 81 mg) for all patients without risk factors for bleeding **(AIII)**, **AND**
	• Anticoagulation for patients who fall under 1 of the following clinical scenarios:
	  • **Therapeutic anticoagulation** for patients with large CAAs according to the American Heart Association guidelines for Kawasaki disease **(AIII)**.
	  • **Therapeutic anticoagulation** for patients with moderate to severe LV dysfunction who have no risk factors for bleeding **(AIII)**.
	  • For patients with MIS-C who do not have large CAAs or moderate to severe LV dysfunction, consider **prophylactic or therapeutic anticoagulation** on an individual basis, taking into consideration risk factors for thrombosis and bleeding. See Table 3e for additional information.

Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.	

[a] The duration of glucocorticoid therapy may vary. When a patient shows clinical improvement (e.g., resolution of fever, improvement of organ function, reduction of levels of inflammatory markers), a steroid taper should be initiated. Typically, the patient's clinical status guides the taper, and it continues for several weeks to avoid rebound inflammation. For more information, see Therapeutic Management of Hospitalized Children With MIS-C, Plus a Discussion on MIS-A.

[b] In certain patients with severe illness, intensification therapy may include dual therapy with higher-dose glucocorticoids plus anakinra **(BIII)** or higher-dose glucocorticoids plus infliximab **(BIII)**. **Anakinra and infliximab should not be used in combination.**

[c] **Infliximab should not be used** in patients with macrophage activation syndrome.

Key: CAA = coronary artery aneurysm; IBW = ideal body weight; IV = intravenous; IVIG = intravenous immunoglobulin; LV = left ventricular; MIS-C = multisystem inflammatory syndrome in children; PO = oral; SUBQ = subcutaneous

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