



## COVID-19

# Special Clinical Considerations

Clinical considerations for care of children and adults with confirmed COVID-19

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## What You Need to Know

- There are additional considerations for people diagnosed with COVID-19 who are pregnant and recently pregnant, children, and people who are moderately or severely immunocompromised, multisystem inflammatory syndrome, and post-COVID-19 conditions. See the NIH Treatment Guidelines on [Clinical Considerations for Special Populations](#) [↗](#).

## Pregnancy and Recent Pregnancy

Pregnant and recently pregnant people (for at least 42 days following the end of pregnancy) are at increased risk of severe illness from COVID-19, including hospital admission, intensive care unit admission, receipt of invasive mechanical ventilation, extracorporeal membrane oxygenation, and death, compared to people who are not pregnant.<sup>(45,46)</sup> Race and ethnicity,<sup>(46-48)</sup> older maternal age, occupation in healthcare, and number and type of underlying conditions are associated with severe COVID-19 illness among pregnant people.<sup>(46,49,50)</sup>

Data from meta-analyses<sup>(51-54)</sup> and observational studies<sup>(50,55,56)</sup> suggest that pregnant people with COVID-19 (compared to pregnant people without COVID-19) are at increased risk of preterm birth and stillbirth and might be at increased risk of pregnancy complications, including pre-eclampsia.

Increased risk for postpartum complications, including hospital readmission, has been observed among recently pregnant people with COVID-19 compared to recently pregnant people without COVID-19.<sup>(57,58)</sup> However, methods for defining the period of recent pregnancy vary from study to study. While some studies include people with COVID-19 immediately after delivery, others include people up to at least 42 days (6 weeks) after a live birth or pregnancy loss.

In general, the therapeutic management of pregnant people with COVID-19 is the same as management of people who are not pregnant. The COVID-19 Treatment Guidelines Panel recommends against withholding treatment for COVID-19 from pregnant or lactating individuals because of theoretical safety concerns. For more information on the treatment of COVID-19 in pregnant people, see the NIH Treatment Guidelines on [Special Considerations in Pregnancy](#) [↗](#).

## Pediatric Populations

The initial clinical presentation of COVID-19 in children can include fever, cough, or other respiratory symptoms; many children also experience gastrointestinal symptoms, including nausea, vomiting, or diarrhea.<sup>(59,60)</sup> Viral tests are recommended for diagnosing COVID-19 in children. Children who develop severe illness can develop abnormal vital signs and

markers of severe inflammation once hospitalized.<sup>(61)</sup> A study of over 10,000 hospitalized children found that lower blood pressure, higher heart and respiratory rates, and abnormal markers of inflammation, including D-dimers and ferritin, were associated with severe illness in children.<sup>(61)</sup>

Studies suggest that many children experience asymptomatic or mild illness, but some children can experience severe COVID-19 illness requiring admission to the hospital or ICU, or use of invasive mechanical ventilation, and some die.<sup>(62)</sup> Like adults, children with underlying medical conditions, including obesity, diabetes, and cardiac, lung, and neurologic disorders have increased risk of severe COVID-19.<sup>(61-64)</sup> Studies of hospitalized children with COVID-19 found that having more than one comorbidity is associated with an increased risk of severe illness<sup>64,65</sup>.

While increasing age is the strongest risk factor for severe COVID-19 illness among adults,<sup>(28)</sup> among children, infants (<12 months of age) may be at increased risk for severe illness.<sup>(66,67)</sup> In addition to individual risk factors, the COVID-19 variant that is circulating at the time of infection could have an impact on disease severity. Compared to prior periods, studies of COVID-19 in the pediatric population during the Delta predominant period found increased rates of hospitalization<sup>(68,69)</sup>; and although the overall number of pediatric hospitalizations was greater during the Omicron predominant period, pediatric patients experienced less severe disease than in previous waves.<sup>(70-72)</sup>

Some of the medications authorized for the treatment of COVID-19 in adults have been authorized for use in children. More information on medications that are authorized for use in children in ambulatory and hospital settings and recommendations for clinical management can be found in the [NIH COVID-19 Treatment Guidelines](#) and the [American Academy of Pediatrics Management Strategies in Children and Adolescents with Mild to Moderate COVID-19](#).

## People who are Moderately or Severely Immunocompromised

People with immunocompromising conditions and people who take immunosuppressive medications or therapies are at increased risk for severe outcomes with COVID-19, including hospitalization, intensive care unit admission, mechanical ventilation, and death.<sup>(73,74)</sup> Studies show that people with a hematologic or solid organ cancer, hematopoietic cell or solid organ transplant, or who are taking immunosuppressive medications, can experience lower vaccine effectiveness than those who are immunocompetent.<sup>(75-77)</sup> However, studies suggest that administration of a third vaccine dose (additional or booster dose) increases immune response and protection against severe illness.<sup>(78-80)</sup> There are additional guidelines about [COVID-19 vaccines, pre-exposure](#) prophylaxis (tixagevimab co-administered with cilgavimab [Evusheld]), [prioritization](#) for therapies, and [treatment](#) specific to this population.

The FDA's [EUAs](#) for several therapeutics, including monoclonal antibodies, the oral antiviral medication [nirmatrelvir with ritonavir \(Paxlovid\)](#), the intravenous antiviral remdesivir, and the oral antiviral [molnupiravir \(Lagevrio\)](#) target this population for early treatment of COVID-19; treatment is best if initiated as soon as possible after diagnosis and within 5 to 7 days after illness onset.

Clinical information on the treatment of patients with immunocompromising conditions can be found on the [NIH Treatment Guidelines for Non-hospitalized Adults](#).

## Management of Conditions Presenting after Acute Illness

### Multisystem Inflammatory Syndrome

Multisystem inflammatory syndrome is a rare but serious post-acute condition that generally occurs 2-6 weeks after SARS-CoV-2 infection and is characterized by systemic inflammation which may affect the heart, lungs, kidneys, brain, skin, eyes, gastrointestinal or other organ systems. Multisystem inflammatory syndrome occurs in children ([MIS-C](#)) and adults ([MIS-A](#)).

### Multisystem Inflammatory Syndrome in Children (MIS-C)

[CDC](#) and the [World Health Organization \(WHO\)](#) have developed case definitions for MIS-C. Both case definitions include clinical criteria including fever, multisystem organ involvement, elevated laboratory markers of inflammation, and history of SARS-CoV-2 infection or exposure to a known COVID-19 case.

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Patients with MIS-C present with fever often accompanied by mucosal or cutaneous lesions, vomiting, diarrhea, abdominal pain, conjunctival hyperemia or injection, and less commonly cough and shortness of breath.<sup>(81,82)</sup> The elevated inflammatory state can lead to the manifestation of severe organ dysfunction<sup>(83)</sup>; in a study of 4,470 pediatric patients with MIS-C in the United States, 80% of patients experienced severe cardiovascular symptoms, 74% mucocutaneous symptoms, 60% severe hematologic symptoms, 44% severe respiratory symptoms, and 25% severe gastrointestinal symptoms.<sup>(82)</sup>

Diagnosing MIS-C can be difficult. The presentation of MIS-C may overlap with that of other conditions, including Kawasaki Disease, toxic shock syndrome, and severe acute COVID-19<sup>83,84</sup>. It is important to consider alternative diagnoses when evaluating children suspected of having MIS-C and to pursue testing to [evaluate multisystem involvement](#) as indicated.

Treatment for patients with MIS-C continues to evolve. A study of over 4,000 patients with MIS-C found that treatment typically includes supportive care and stabilization of the patient, immunomodulatory treatment (including IVIG, steroids, and/or other medications), and anticoagulant and antiplatelet therapy.<sup>(85)</sup> Clinical treatment guidelines for MIS-C that describe diagnosis and clinical treatment options have been developed by the [American College of Rheumatology](#), the [National Institutes of Health](#), and the [American Academy of Pediatrics](#). For clinical information to assist providers in speaking with patients and families about MIS-C, see [Talking with Families and Caregivers](#).

## Multisystem Inflammatory Syndrome in Adults (MIS-A)

CDC provides a [case definition for MIS-A](#). Patients with MIS-A are often young adults who present with fever, elevated laboratory markers of inflammation, hypotension or shock, cardiac dysfunction, shortness of breath, and gastrointestinal symptoms.<sup>(86,87)</sup>

As with MIS-C, diagnosing MIS-A can be challenging because patients may have experienced an asymptomatic or mild initial SARS-CoV-2 infection, which may have been undiagnosed, and signs and symptoms of MIS-A overlap substantially with those of acute COVID-19 in adults.<sup>(87)</sup> Similar to MIS-C, it is important to consider alternative diagnoses and to evaluate for multisystem involvement.

Treatment recommendations have not yet been developed for MIS-A; however, studies have reported the use of steroids, intravenous immunoglobulins (IVIG), other immunomodulatory medications, and supportive care for treatment.<sup>(86,87)</sup>

Consider reporting cases of MIS-C or MIS-A to your local, state, or territorial health department. Data concerning health department-reported cases of MIS-C in the United States are available in [CDC COVID Data Tracker](#).

## Post-COVID Conditions or Long COVID

[Post-COVID conditions](#) refer to a range of new or persistent symptoms and health conditions that may affect multiple organ systems and are present 4 or more weeks after SARS-CoV-2 infection.

Commonly reported symptoms include fatigue, post-exertional malaise, dyspnea, anxiety or psychological distress, joint or muscle pain, cough, chest pain, cognitive impairment, and headache.<sup>(88,89)</sup> Patients with post-COVID conditions can also be diagnosed with new conditions, including diabetes and mental health concerns.<sup>(88)</sup> Diagnosis of post-COVID conditions can be difficult because the symptoms are associated with many medical conditions. Clinicians can consult CDC's [General Clinical Considerations](#) for suggestions on initial diagnostic and follow-up evaluation when caring for patients with post-COVID conditions. When patients experience symptoms 4 weeks or more after SARS-CoV-2 infection, clinicians may consider alternative diagnoses, as well as post-COVID conditions, and complete additional follow-up visits as indicated by on-going need.

Several factors, including severity of initial COVID-19 infection, pre-existing medical conditions, older age, infection without vaccination, and female sex have been found to be associated with an increased occurrence of post-COVID conditions.<sup>(90-92)</sup> Estimates of the proportion of people who had COVID-19 that go on to experience post-COVID conditions range widely; in

studies of post-COVID conditions that use uninfected comparison groups, estimates are lower.<sup>(88,89,93)</sup> A large cohort study of veterans in the U.S. estimated that the overall burden of Long COVID beyond the first 30 days of illness is nearly 7%, and more than 20% among patients who were hospitalized.<sup>(92)</sup>

Children experience post-COVID conditions, but they appear to be affected less frequently than adults. Estimates of the proportion of children who experience COVID-19 and later develop post-COVID conditions range widely.<sup>(94)</sup> School-based studies suggest that post-COVID conditions can occur in 1–4% of children infected with SARS-CoV-2, but in some reports of children who were previously hospitalized during acute COVID-19 infection, estimates of post-COVID conditions can be as high as 25%.<sup>(95,96)</sup> Rates of post-COVID conditions seem to increase with age among children and adolescents.<sup>(94)</sup>

Many patients diagnosed with post-COVID conditions slowly improve over several months, but some studies suggest that patients can experience prolonged illness lasting more than 6 months.<sup>(97,98)</sup>

Post-COVID conditions are challenging to study because they include a wide range of physical and mental health consequences that are new, returning, or ongoing. Studies to date include different patient populations, and assessments at varying points of time after acute infection; many studies include only one assessment or do not include control groups; and the severity and impact of symptoms on quality of life or daily activities have not been consistently reported.

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- [Information about COVID-19 Vaccines for People who Are Pregnant or Breastfeeding](#)
- [Considerations for Inpatient Obstetric Healthcare Settings](#)
- [Care for Breastfeeding People](#)
- [Breastfeeding and Caring for Newborns if you Have COVID-19](#)
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### MIS

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- [MIS-C Healthcare Provider Resources](#)
- [Information for Healthcare Providers about MIS-C](#)
- [MIS-C Information for Healthcare Providers About Talking with Families and Caregivers](#)
- [IDSA Multisystem Inflammatory Syndrome in Adults](#) 
- [MIS-C Cases in the United States](#)

### Post-COVID Conditions

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