SARS-CoV-2 Infection and COVID-19 in Children

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KEYWORDS

• COVID-19 • Pediatrics • SARS-CoV-2 • Children • MIS-C

KEY POINTS

- Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) prevalence is high in pediatric populations, especially during the Omicron variant and subvariant waves.
- Clinical manifestations of coronavirus disease 2019 (COVID-19) are generally less severe than in adults, although severe disease can occur in high-risk individuals.
- Multisystem inflammatory syndrome in children is a unique post-COVID phenomenon that occurs rarely, mostly in children approximately 1 month after acute SARS-CoV-2 infection.
- SARS-CoV-2 vaccination remains crucial to prevent severe disease in children.
- Treatment considerations generally follow recommendations for adults and older adolescents should be managed similarly to adults.

EPIDEMIOLOGY

Several databases are available to determine the burden of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19) in pediatric populations. The COVerAGE database (COVerAGE-DB), an open-access database from more than 103 countries, recorded 56.9 million COVID-19 cases children and adolescents aged less than 20 years with a prevalence range from 0% to 37% of the national caseload across countries.[1] Of these, 63% occurred among adolescents aged 10 to 19 years, and 37% occurred among children aged 0 to 9 years. The Pediatric COVID-19 case registry, the largest registry in the United States, collected information from 12,917 children with COVID-19 during the first year of the pandemic.[2] Infections were most common among those 12 to 18 years of age (31%), followed by 5 to 11 years of age (24%) with no significant difference in gender. Most cases were in White Caucasians followed by in Blacks. One in 4 cases was in Hispanic/Latinos. Reported COVID-19 cases in children increased significantly in 2022 during the Omicron surge. In the United States alone, more than 5 million of a total 13 million cases were diagnosed between January 1, 2022 and May 12, 2022, and the percent of total cases occurring in children increased from 10% to 30%.[3–5] As of February 2022, almost 75% of children and adolescents had serologic evidence of previous infection with SARS-CoV-2, with approximately one-third becoming newly seropositive since December 2021 with the highest in the age group with lowest vaccination rates (5–11 years, 28%).[6]

Most children seem to have asymptomatic, mild, or moderate disease and recover within 1 to 2 weeks of disease onset.[7–9] However, children with COVID-19 may develop severe complications, such as respiratory distress syndrome, myocarditis, acute renal failure, and multisystem organ failure.[10–14] Around 0.1% to 1.5% of pediatric COVID-19 patients require hospitalization, representing close to 5% of all pediatric hospitalizations in the United States.[3] Age, race,

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and ethnicity have been described as risk factors for hospitalization with the highest rates seen in those aged younger than 12 months, Hispanics, and non-Hispanic Black children.[15–20] The annual COVID-19-associated hospitalization rate by age is shown in **Table 1**. Among children hospitalized with COVID-19 in the United States, between 28% and 40% required intensive care unit (ICU), 6% to 18% needed invasive mechanical ventilation, and up to 3% died.[21,22]

SARS-CoV-2-related death in children and adolescents is rare.[23,24] On February 2021, a pooled analysis from Europe and the US estimated COVID-19-associated death in children to be 0.17 per 100,000.[4,25] Among the 4.4 million COVID-19 deaths reported in the COVerAGE-DB, more than 17,200 (0.4%) occurred in children and adolescents aged younger than 20 years, with 53% among adolescents aged 10–19 years, and 47% among children aged 0–9 years.[1] Case fatality ratios (CFRs) have varied among continents over time. Although Asia had the highest CFR initially, Europe, and North America, followed by South America surpassed those of Asia shortly after a pandemic was declared. High-income countries had an exponential increased in their CFRs compared with low-income countries probably due to underreporting and lower testing capacities from low-income countries.[26] Specifically, the percentage of COVID-19 mortality in those aged younger than 20 years, varied among countries based on income: high-income (0.1), upper-middle-income (0.6%), low-middle-income (1.2%), and low-income (0.9%) countries.[1] Cumulative mortality rates for the United States are shown in **Table 1**.

RISK FACTORS FOR SEVERE DISEASE

Our understanding of COVID-19 severity in children has evolved over time. Although children with certain underlying medical conditions are at increased risk for severe illness (hospitalization, need for intensive care or mechanical ventilation, death) evidence associating specific conditions is limited. In addition, children without comorbidities can also experience severe COVID-19.[11,15,17,18,27–32]

In children aged younger than 2 years, chronic lung disease, neurological disorders, cardiovascular disease, prematurity, or airway abnormalities are associated with an increased risk for severe COVID-19.[33] Among children aged 2 to 18 years, obesity, diabetes, and feeding tube dependence carried significant risk for severity (**Box 1**). Individuals with sickle cell disease, due to underlying cardiopulmonary comorbidities, are more likely to be hospitalized, develop pneumonia, and present with hypoxemia due to COVID-19. However, mortality has not been significantly different across studies.[34–37]

There are conflicting reports on whether immunocompromised individuals, including recipients of solid organ or hematopoietic cell transplants, are at higher risk for severe diseases.[38–45] Although some of these differences have been adjudicated to lower threshold for hospital admission in children with these conditions, Mukkada and colleagues[43] showed that cancer is independently associated with severe disease. In their cohort, one-fifth of children and adolescents with cancer experience severe COVID-19, and deaths occurred in a higher proportion than is reported for those without comorbidities. Specifically, in patients aged 15 to 18 years, severe lymphopenia and intensive chemotherapy were independently associated with disease severity.[43]

Lack of vaccination is the most important modifiable risk factor for severe disease. Among 400 children hospitalized for COVID-19 during the Omicron wave, 9 in 10 were unvaccinated COVID-19-associated hospitalization rates among unvaccinated children aged 5 to 11 years were twice as high as rates in children vaccinated with a primary series (19 vs 9 per 100,000).[46] Similar results have been reported for those aged 12 to

Table 1
Clinical outcomes by age in pediatric patients with coronavirus disease 2019

Age	Annual Hospitalization Rate per 100,000[4,133]	Overall Cumulative Mortality per Million[134]
Overall (<18 y)	48.2	18.4[a]
0–4 y	66.8	<12 mon: 80.6 1–4 y: 9.1
5–11 y	25	6.9
12–17 y	59.9	17.8
18–19 y		48.5

[a] Range 0–19 y.

Box 1
Risk factors for severe coronavirus disease 2019 disease in children

Risk factors

- Asthma or other chronic pulmonary diseases
- Obesity[a]
- Diabetes mellitus
- Congenital heart disease/cardiovascular disease
- Sickle cell disease
- Neurologic conditions
- Metabolic conditions
- Genetic conditions
- Medical complexity
- Immunosuppression

[a]Body mass index [BMI] greater than 95th percentile for age and sex.

17 years, in whom the rates of hospitalization among unvaccinated were 2.5× higher when compared with vaccinated teens.[47] This data is further supported by studies from adults showing the impact of vaccination in preventing severe disease, hospitalization, and death.

CLINICAL MANIFESTATIONS

The clinical presentation of COVID-19 in children is diverse and varies by age. Asymptomatic infection in children ranges from 10% to 42%.[8] The most common symptoms in children are fever and cough, followed by shortness of breath, sore throat, headache, myalgia, fatigue, and, less frequently, rhinorrhea.[38,48–50] Studies limited to infants have shown that poor feeding with fever in the absence of obvious signs can be part of the clinical presentation. In addition, several groups have described SASR-CoV-2-associated bronchiolitis.[51] There is less evidence on the clinical presentation of COVID-19 in immunocompromised children. The Pediatric COVID-19 case registry has 614 immunocompromised patients and 12,309 immunocompetent children.[2] Asymptomatic infection was seen in almost 40% of immunocompromised children compared with around 20% in immunocompetent children (**Table 2**). **Box 1**

In an international registry of 1500 children with cancer, asymptomatic infection was reported in one-third, with fever and cough being the most common symptoms in those who became sick.[43] Rhinorrhea and stuffy nose and gastrointestinal (GI) symptoms were reported in 10% of cases and tachypnea, sore throat, body aches, and headaches in 5% to 7%. Anosmia, ageusia, chills, and cutaneous manifestations were seen in less than 3% of the patients. Similar results have been reported by others.[40–44,52]

SARS-CoV-2 produces heterogeneous respiratory involvement in children. The vast majority has mild upper respiratory tract symptoms. However, progression to the lower respiratory tract has been well described, with pneumonia being the most frequent manifestations and acute respiratory distress syndrome the most severe one.[27,49,53,54] Chest radiograph imaging is the first preferred method to assess children with suspected pneumonia. Radiologic abnormalities can be present in about half of the patients with dyspnea and differ from that observed in adults. They can be unilateral or bilateral, single, or multiple, and most seen in the lower lobes. Unilateral increased density and bilateral peribronchial changes are commonly seen. Ground-glass opacities and patchy shadowing on a chest computerized tomography (CT) scan are the most recognized signs in children.[55–64] Less common manifestations including single-round consolidation, pleural effusion, small nodules, or lymphadenopathy have been reported. According to the US COVID-19 pediatric registry, abnormal findings on pulmonary imaging. (**Table 3**) during the first week of disease were most seen in immunocompromised children, with the most common radiologic findings being multifocal or patchy opacities, followed by interstitial infiltrates and bronchial thickening.[2]

Although COVID-19 affects mainly the lungs, extrapulmonary manifestations affecting several systems have been described in adults as well as in children. Myocarditis, pericarditis, heart failure, and arrhythmias have been described in children and adolescents.[65] The risk of myocarditis and myocarditis or pericarditis associated with SARS-CoV-2 infection varies by age and gender but is overall low and higher than after mRNA vaccination. The highest incidence is seen in boys aged 12 to 17 years (50.1–64.9 cases per 100,000) followed by boys 5 to 11 years (12.6–17.6 cases per 100,000).[66–68] Cardiac manifestations in children with preexisting heart conditions do not significantly differ from those without cardiac disease; however, SARS-CoV-2 can worsen the basal status of this population.[69]

Neurological manifestations are frequent and vary in severity. Between 20% and 40% of children hospitalized with COVID-19 had one or more neurological symptom, affecting the central and/or peripheral nervous system.[70–72] As with cardiac

Table 2
Frequency of symptoms in immunocompetent and immunocompromised children in the US COVID-19 pediatric registry[2]

		Day 0			
		General Pediatric, n = 12309		Immunocompromised, n = 614	
Symptoms	Yes	9554	77.62%	383	62.38%
	No	2670	21.69%	229	37.30%
Fever		5362	43.56%	227	36.97%
Cough		4590	37.29%	186	30.29%
Rhinorrhea		2983	24.23%	105	17.10%
Headache		2584	20.99%	74	12.05%
Sore throat		2223	18.06%	48	7.82%
Decreased oral intake		1784	14.49%	74	12.05%
Myalgia		1612	13.10%	61	9.93%
Vomiting		1528	12.41%	61	9.93%
Lethargy		1346	10.94%	56	9.12%
Shortness of breath		1239	10.07%	71	11.56%
Diarrhea		1181	9.59%	66	10.75%
Abdominal pain		1167	9.48%	49	7.98%
Nausea		1082	8.79%	55	8.96%
Loss of smell/taste		958	7.78%	35	5.70%
Chest pain		558	4.53%	27	4.40%
Rash		472	3.83%	6	0.98%
Conjunctivitis		337	2.74%	6	0.98%
Wheezing		259	2.10%	8	1.30%
Seizure		172	1.40%	5	0.81%
Apnea		54	0.44%	1	0.16%
Hypothermia		32	0.26%	4	0.65%
Hemoptysis		19	0.15%	1	0.16%

Data from Pediatric COVID-19 Case Registry. Accessed June 28th, 2022. https://www.pedscovid19registry.com.

manifestations, CNS involvement can be seen in the acute phase or as part of multisystem inflammatory syndrome in children (MIS-C).[70] The vast majority of these are transient and fully resolve over time. In addition to anosmia and ageusia, common manifestations are headache, encephalopathy, seizures, and weakness. Children with preexisting neurological disease could experience exacerbation and/or progression of their underlying condition, especially those with neuromuscular disease.

Dermatologic manifestations include the vasculitic chilblain-like acral pattern of the distal toes, consisting of reddish-purple nodules on the distal digits and often refer as "COVID toes" and have been described more frequently in children and young adults.[73]

The most common GI symptoms in children with COVID-19 are vomiting and diarrhea, followed by anorexia, abdominal pain, and poor appetite.[48,74–76] GI symptoms can be the first manifestation of COVID-19 and can occur with or without respiratory symptoms.[77,78] Although most of these are self-limited, a Spanish multicenter study showed that children with COVID-19 and GI symptoms had more severe disease than those without GI symptoms.[79] Of note, children with GI symptoms required careful monitoring given that vomiting, abdominal pain, and/or diarrhea can be a manifestation of MIS-C.

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

MIS-C has been most frequently described in children aged from 1 to 14 years and is most prevalent in children aged older than 5 years.[80] Since first reported in England in April 2020, several studies have reported cases of MIS-C with peaks that lag the peak of acute COVID-19.[81–86] These have led

Table 3
Pulmonary findings during the first week of diagnosis with coronavirus disease 2019 in immunocompetent and immunocompromised children in the US COVID-19 pediatric registry[2]

Finding	Day 0			
	General Pediatric, n = 12309		Immunocompromised, n = 614	
Abnormal XR	911	7.40%	82	13.36%
Bronchial or peribronchial thickening/cuffing	270	2.19%	10	1.63%
Interstitial infiltrates	188	1.53%	14	2.28%
Lobar consolidation	86	0.70%	10	1.63%
Multifocal or patchy opacity	456	3.70%	52	8.47%
Abnormal CT	82	0.67%	21	3.42%
Bronchial or peribronchial thickening/cuffing	4	0.03%	1	0.16%
Interstitial infiltrates	4	0.03%	2	0.33%
Lobar consolidation	13	0.11%	2	0.33%
Multifocal or patchy opacity or ground glass opacity	53	0.43%	12	1.95%
Nodule(s)	9	0.07%	4	0.65%
Tree-in-bud opacities	1	0.01%	0	0.00%

Data from Pediatric COVID-19 Case Registry. Accessed June 28th, 2022. https://www.pedscovid19registry.com.

to the hypothesis that MIS-C is an immune-mediated port infectious complication of SARS-CoV-2. The incidence of MIS-C early in the pandemic was 1 case per 3000 infections in individuals aged younger than 21 years.[87] To date, more than 8525 cases and 69 deaths have been reported in the United States. The median age of patients with MIS-C was 9 years. Half of children with MIS-C were aged between 5 and 13 years and 61% were boys.[80] Almost 60% of the reported patients with race/ethnicity information available (N = 8038) occurred in children who are Hispanic/Latino or Black, non-Hispanic.[80,88] The most common manifestations are persistent fever and GI symptoms such as abdominal pain, vomiting, and diarrhea. Individuals can also have mild-to-moderate respiratory symptoms, rash, conjunctivitis, mucous membrane involvement, and neurocognitive impairment. Respiratory failure, as seen in acute COVID-19, is not a common characteristic of MIS-C.[83,84,89–91] Cardiac involvement is commonly and can include acute myocardial dysfunction, arrhythmias or conduction abnormalities, and coronary artery dilation.[92–94] Several laboratory abnormalities have been associated with MIS-C including increased in inflammatory markers such as c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, fibrinogen, and D-dimer. Troponin and brain natriuretic peptide are often elevated. Both The Centers for Disease Control and Prevention (CDC) and The World Health Organization (WHO) have defined criteria to diagnose MIS-C that includes clinical presentation, laboratory finding, and organ involvement.[89,90] MIS-C shares characteristics with Kawasaki disease (KD); however, MIS-C affects older children and disproportionally affects Black and Hispanic with very few cases described in Asian children. In addition, GI symptoms are more common and prominent in MIS-C, and inflammatory markers tend to be higher when compared with KD.[95–97] Although these distinctions can be helpful, ultimately, a previous history of SARS-CoV-2 infection or known COVID-exposure will aid in determining MIS-C or KD.[89,90] Although the course of MIS-C can be severe, requiring intensive care support, outcomes are overall good with most children recovering. However, deaths have been reported, and long-term outcomes in those who have recovered have not been properly studied.[80,83,84,98,99]

Post-COVID Conditions

The phenomenon of persistent symptoms following COVID-19 has been variably termed long COVID, long-haul COVID, postacute sequelae of COVID-19, post-COVID, and COVID syndrome. The WHO defines post-COVID-19 conditions as occurring in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months

and cannot be explained by an alternative diagnosis.[100] Importantly, the WHO specifies that a separate definition may be applicable to children. The CDC definition of post-COVID-19 conditions includes a wide range of health consequences that are present 4 or more weeks after infection with SARS-CoV-2.[101] Overall, post-COVID-19 conditions in children seem to be less common than in adults. An early publication from a national survey in the United Kingdom estimates that 7% to 8% of children may experience continued symptoms for over 12 weeks. The most common symptoms are fatigue, headache, insomnia, trouble concentrating, muscle and joint pain, and cough and can occurred after infection, irrespective of its severity, or MIS-C. These symptoms can limit physical activity, cause distress about symptoms, decrease school attendance/participation, and become mental health challenges.[102,103] A systematic review of 21 studies that included children and adolescents found a 25.24% prevalence of long-COVID, with mood symptoms, fatigue, and sleep disorders most commonly reported.[104] Other studies have reported varying ranges of persistent symptoms after COVID. A Danish study reported higher rates of symptoms at 2 months postinfection in children aged 0 to 14 years compared with controls in a cross-sectional case-control study,[105] whereas an international study of ~1800 children demonstrated very low prevalence of symptoms at day 90.[106]

Several factors may influence the reported prevalence of prolonged symptoms in children and the apparent discrepancy among various studies. Namely, stratification by age, gender, vaccination status, and viral variant are likely needed to fully characterize the effect. Initial data has suggested that the risk of long COVID is reduced in individuals that had received 2 doses of vaccine[107,108]; however, data specific to children and with newer variants are currently lacking. Infection with different viral variants, especially Omicron, is likely to influence the risk of long COVID[109]; however, data in children are not yet available.

Treatment

Systematic data on the use of specific treatments for COVID-19 in pediatric patients remain limited. Through some clinical trials of COVID-19 therapeutics allowed inclusion of adolescents, adolescent enrollment in most trials was low and sometimes nonexistent. Nonetheless, several agents are now approved and/or have emergency use authorization for use in children and adolescents. As the landscape of therapeutics continues to change and new data become available, recommendations are likely to also change. Guidelines from the Infectious Diseases Society of America (https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/) and the National Institutes of Health (https://www.covid19treatmentguidelines.nih.gov/) are updated regularly and provide up-to-date reviews of currently available data.

Remdesivir

Remdesivir is approved by the FDA for use in hospitalized and nonhospitalized pediatric patients aged 28 days or older and weighing 3.0 kg or greater.[110] Remdesivir for use in early infection was evaluated in nonhospitalized, high-risk adults with mild-to-moderate disease, where a 3-day infusion was associated with an 87% risk reduction of hospitalization or death.[111] Only 8 adolescents aged younger than 18 years were included in the trial; however, current guidelines recommend consideration of use in nonhospitalized children or hospitalized children not on oxygen, aged 12 years or older who are at high risk of progression to severe COVID-19.[112] Children aged younger than 12 years can be considered for remdesivir as well, although data are lacking. The efficacy of remdesivir in hospitalized individuals is limited to trials involving adult subjects.[113–116] Interim results of a phase 2/3, single-arm, open-label study aimed at evaluating the safety, tolerability, and pharmacokinetics of remdesivir in children demonstrated overall acceptable safety profile,[117] although the lack of a placebo group in this trial limits the evaluation of efficacy. Remdesivir thus is recommended for pediatric patients who have a new or increasing oxygen need.

Ritonavir-boosted nirmatrelvir (paxlovid)

The FDA issued an emergency use authorization (EUA) for ritonavir-boosted nirmatrelvir for nonhospitalized individuals with mild to moderate COVID-19 aged ≥12 years and at high risk for progression to severe disease.[118] Efficacy, however, has only been demonstrated in adults, where an 89% relative risk reduction was found compared to placebo.[119] Given the efficacy data in adults, ritonavir-boosted nirmatrelvir is recommended for adolescents aged 12 years or older who are at high risk of progressing to severe disease.[112] Importantly, drug interactions must be considered when administering ritonavir-boosted nirmatrelvir, which may prevent use in certain high-risk populations such as immunocompromised children.

Monoclonal antibodies

Several monoclonal antibodies (mAbs) have been developed and received EUAs for adults and children aged 12 years or older; however, emergence

of SARS-CoV-2 variants has rendered most mAbs ineffective for use as treatment. Currently, bebtelovimab is the only mAb available for use that has maintained in vitro activity against Omicron subvariants.[120] No clinical data is available in either adults or children demonstrating efficacy, thus, despite the EUA for use in nonhospitalized patients, current guidelines do not recommend for or against use in children aged 12 years or older who have mild-to-moderate COVID-19 with high risk of progression to severe COVID-19. Up-to date guidance on activity of different mAbs against circulating SARS-CoV-2 variants can be found at https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/. The use of mAbs for prophylaxis is discussed below.

Corticosteroids and other immunomodulators

In general, despite lack of systematic data on use, recommendations for corticosteroid use in children with COVID-19 follow recommendations in adults. The benefits of corticosteroids have been demonstrated in several clinical trials, including the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial where a mortality benefit was observed in adults with COVID-19 on supplemental oxygen receiving dexamethasone.[121] Given overall lower mortality in children, and that the strongest effect was seen in patients on higher levels of oxygen support, dexamethasone is reserved for children requiring high flow or more supplemental oxygen.[112] Several other immunomodulators have been evaluated in adults with moderate to severe COVID-19, including baricitanib, tofacitinib, and tocilizumab.[122–127] Without pediatric efficacy data, potential benefits of these therapies must be extrapolated from adult studies, and therefore, the use is limited to patients with severe COVID-19 (noninvasive and invasive mechanical ventilation).[112]

Prevention and Prophylaxis

Vaccination

The mainstay of prevention of severe COVID-19 in children is vaccination. Currently 2 mRNA vaccines (Pfizer/BioNTech, Moderna) and 1 protein subunit vaccine (Novavax) are either approved or hold EUA status for children in the United States. Both the Pfizer-BioNTech and Moderna vaccines are authorized down to 6 months of age, whereas the Novavax vaccine is authorized down to 12 years of age. Up to date dosing schedules for primary series and booster doses can be found at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html#recommendations. Vaccine effectiveness estimates for children have varied by vaccine dosing regimens, history of prior infection, and SARS-CoV-2 variant predominance[128]; however, protection against severe disease remains an important clinical endpoint. The American Academy of Pediatrics and the Advisory Committee on Immunization Practices recommend vaccination (including booster doses) for all children aged 6 months or older.[129,130]

Monoclonal antibodies for preexposure and postexposure prophylaxis

As outlined above, emergence of SARS-CoV-2 variants has resulted in several mAbs being no longer effective for both treatment and prophylaxis. Prophylaxis with mAb is generally reserved for those that are unable to mount an adequate response to vaccination, namely individuals that are moderately to severely immunocompromised. Tixagevimab 300 mg plus cilgavimab 300 mg (Evusheld) is the only available mAb combination currently available for use as preexposure prophylaxis against SARS-CoV-2 for adults and adolescents aged 12 years or older with moderate-to-severe immunocompromise or in individuals unable to be fully vaccinated due to history of severe adverse reactions to COVID vaccines.[112] Of note, current dosing guidance, including repeat dosing at 6 months, are not based on clinical trial data therefore data on efficacy is limited, especially in pediatrics.[131,132] No mAbs are currently approved for postexposure prophylaxis; however, this may change as new variants and mAbs emerge.

SUMMARY

Although our knowledge of COVID-19 has significantly evolved over the course of the pandemic, COVID-19 continues to be an important health problem around the world. We have a better understanding of the various clinical presentations and risks factors for severe disease. We have access to accurate diagnostics tests and limited, yet effective therapies targeting the virus or modulating the immune response to it. Vaccines, which continue to prove safe and effective, are now available for anyone aged 6 month and older. However, lack of access, inequity, disinformation, and vaccine hesitancy have led to disparities in vaccination rates among countries, enabling the virus to mutate and leaving all of us vulnerable to new surges. Particularly vulnerable, are children, who have the lowest vaccination rates and have been increasingly affected with each new wave driven by a different variant of concern. Scientifically we have made remarkable and unprecedented progress and while many answers

lay ahead, we will undoubtedly be able to answer them. However, the biggest questions, is whether we will be able to bring drown the social and economic disparities needed to overcome this pandemic.

CLINICS CARE POINTS

- Although severe COVID-19 is less frequent in children, the direct and indirect effects of COVID-19 on children's health continues to be substantial.
- Vaccines against SARS-CoV-2 are available for everyone 6 months of age and older. They have been proven to be safe and effective in reducing the risk of severe disease.

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