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After studying this article, you should be able to:

 Monitor children and adolescents for symptoms of long COVID using multidisciplinary approaches

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# and Adolescents

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#### ABSTRACT

**Objective:** To review the empirical evidence regarding neuropsychiatric illness (long coronavirus disease [COVID]) in children and adolescents postsevere acute respiratory coronavirus disease 2 (SARS-CoV-2) infection.

Data Sources: A search of PubMed, PsycINFO, Cochrane Library, and Google Scholar was conducted from the date of inception until February 2022 using the keywords corona\*, COVID-19, SARS-CoV-2, mental health, depression, anxiety, neurological, psychiatric, long COVID, and post-COVID outcomes. Age filters were used to include children and adolescents aged  $\leq$  18 years.

Study Selection: The search resulted in the identification of 526 articles; 48 articles met the inclusion criteria.

Data Extraction: Results are presented using a narrative review format. Data regarding long COVID in children and adolescents post-SARS-CoV-2 infection were extracted to understand epidemiologic trends, preventive measures, and treatment options.

Results: Studies during the initial phase of the pandemic reported a mixed range of symptoms from case reports or case series. However, multisystem inflammatory syndrome in children (MIS-C) was widely reported. During the subsequent phases, the emergence of new variants led to a surge of SARS-CoV-2 infections in pediatric populations. There were highly variable, mixed symptom clusters within 60 days post-infection, which resolved in many patients within 6 months. There were prolonged illnesses and impairments in some children and adolescents with long COVID, and many had similar symptoms even though they tested negative for COVID-19.

Conclusions: Long COVID symptoms are both physical and mental in nature among children and adolescents. The impairments have the potential to affect long-term functioning and increase the overall burden on health care delivery. Despite current studies having methodological issues, there is a consensus to provide multidisciplinary and holistic care to those in need.

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n children, coronavirus disease 2019 (COVID-19) is often A asymptomatic (43%-68% of cases) or causes mild symptoms, and life-threatening illness or death from COVID-19 is rare.<sup>1</sup> The extensively studied indirect effects of the COVID-19 pandemic on the mental health of children and adolescents have multiple predisposing and perpetuating factors including social isolation, increased screen time, lack of physical activity, heightened perceived risks, and parenting stress.<sup>2</sup> These factors attributed to a surge in It is illegal to post this copyrighted PDF on any website.

#### **Clinical Points**

- Long COVID in children and adolescents is a distinct clinical condition that presents in relapsing and remitting patterns and is recognized cross-culturally with a mixed range of highly variable symptoms within 60 days of SARS-CoV-2 infection.
- Many who tested negative for COVID-19 also had long COVID symptoms with impairments similar to those who tested positive.
- Epidemiology, risk factors, and mechanisms are largely unknown, and although most children and adolescents recover from long COVID within 6 months, many suffer from persistent illness and impairments.
- Vaccinations may play a role in prevention of long COVID in children and adolescents, and multidisciplinary specialized COVID rehabilitation clinics are a step in the right direction.

mental health emergency visits, self-reports of symptoms of anxiety, depression in adolescents, and externalizing disorders among college-aged youth.

During the initial phase of the pandemic, children and adolescents were considered largely spared from the direct effects of COVID-19 infection, with very limited morbidity and mortality.<sup>3</sup> According to the American Academy of Pediatrics, less than 1.5% of child cases have resulted in hospitalization. The neuroinvasive potential of coronaviruses has been previously described for severe acute respiratory syndrome coronavirus (SARS-CoV),<sup>4</sup> Middle East respiratory syndrome coronavirus,<sup>5</sup> human coronavirus 229E,<sup>6</sup> and human coronavirus OC43.<sup>7</sup> The increased risk of neuropsychiatric implications may be attributed to viral infiltration of the central nervous system (CNS), dysregulation of the cytokine network, hypercoagulable states, transmigration of peripheral immune cells, and post-SARS-CoV-2 infection autoimmune effects.8

After a positive test for COVID-19, 13.3% of adults had a cluster of symptoms that lasted for at least 4 weeks and 4.5% for at least 8 weeks.<sup>9</sup> These symptoms<sup>10</sup> of brain fog, cognitive dysfunction, headache, loss of taste and smell, emotional and mood fluctuations, memory loss (both short term and long term), encephalopathy, cerebrovascular disease, sleep disturbance, and hallucinations were termed long COVID (also called post-COVID-19 condition, post-acute sequelae of COVID-19, or chronic COVID syndrome).<sup>10,11</sup> The World Health Organization defines long COVID in adults as "people with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19, with symptoms that last for at least 2 months and cannot be explained by alternative diagnoses."<sup>12(p3)</sup> The neurologic and psychiatric manifestations are observed in 20%-35% of adult patients.<sup>13–15</sup> There are studies<sup>16,17</sup> in adults on the overall epidemiology, risk factors, and preventive measures (vaccinations) and treatments, but the data in children are largely missing.

Despite reports of a significant increase in SARS-CoV-2 infection in children and adolescents, there is very limited The highly transmissible Omicron coronavirus variant in children and adolescents makes up about 5% of all COVID-19 hospitalizations, which is up to 4 times higher than that of previous COVID waves.<sup>18</sup> The Omicron variant replicates 70 times faster in human airways and has a harder time multiplying in lung tissue than the Delta variant, suggesting why it might cause less severe disease, but clinicians still worry that infected individuals might develop long COVID. In 2020, several studies<sup>19-22</sup> started to report neuropsychiatric sequelae post-SARS-CoV-2 infection in adults; however, it was not until 2021 that long COVID cases were reported among children and adolescents.

For children and adolescents, there are many questions regarding long COVID and the prevalence, risk factors, and plausible molecular, immunologic, and psychological mechanisms for its long-term effects. The objective of this article is to review the literature on long COVID in children and adolescents post-SARS-CoV-2 infection to understand epidemiologic trends, preventive measures, and treatment options.

#### **METHODS**

A comprehensive search of several databases was conducted from the date of inception to February 2022. The databases included PubMed, PsycINFO, Cochrane Library, and Google Scholar. The search was designed using the following controlled vocabulary and keywords: corona\*, COVID-19, SARS-CoV-2, mental health, depression, anxiety, neurological, psychiatric, long COVID, and post-COVID outcomes. Age filters were used to include children and adolescents aged  $\leq$  18 years. The search was performed in all languages and was limited to human subjects. A manual search of references in included studies was performed to avoid selection bias. Reverse citations were also reviewed to update the material. Research articles that focused exclusively on the association between COVID-19 infection in children and adolescents and mental health in individuals aged  $\leq$  18 years were selected for review. The inclusion criteria were any published material on individuals aged  $\leq$  18 with COVID-19 who reported symptoms of any psychiatric manifestations including depression, anxiety, insomnia, or psychosis. After the removal of duplicates, 526 articles were identified, and 48 articles met the inclusion criteria.1-3,11,13,18,23-65

#### RESULTS

There is limited empirical evidence about neuropsychiatric symptoms post-SARS-CoV-2 in children and adolescents. The studies included in this review are from diverse populations, including the United Kingdom, Sweden, Norway, Denmark, the United States, Italy, France, Tanzania, and Argentina. More recent studies were also included since the Delta and subsequent variants led to a surge in cases among children and adolescents. These were

Study	Illness Type	Study Characteristics	Key Findings	
Buonsenso et al (2021) <sup>25</sup>	Neuropsychiatric	510 children, mean age of 10.3 y with COVID-19 symptoms for more than 4 wk, United States and United Kingdom	The persisting neuropsychiatric symptoms of lack of concentration (60.6%), difficulty remembering information (45.9%), doing everyday tasks (40%), and processing information (32.7%) and short-term memorissues were reported.	
Ludvigsson (2021) <sup>26</sup>	Neuropsychiatric	5 children with long COVID (4 girls), median age of 12 y, Sweden	Headache, difficulty in concentrating, brain fog, and memory loss were observed.	
Hutchison et al (2020) <sup>33</sup>	MIS-C	1 boy, age 14 y, United States	Agitation, short-term memory impairment, difficulty in concentration, and lack of attention were observed during the period of hospitalization	
Pavone et al (2021) <sup>28</sup>	PANS	2 boys, aged 12 y and 13 y, Italy	The first child presented symptoms of OCD, emotional lability, facial motor tics, and lack of attention over a period of 2 months post- infection; the second child presented facial motor tics, guttural vocal tics, hyperactivity, aggressiveness, irritability, inattentiveness, and lack of appetite with no significant improvement after 1 month.	
Nathan et al (2020) <sup>29</sup>	Neurologic	5 infant boys, aged $\leq$ 3 month	Neurologic symptoms were observed in the patients at admission, which included axial hypotonia or drowsiness and moaning sounds or both.	
Lindan et al (2021) <sup>30</sup>	Neuropsychiatric	38 children with neurologic disease related to SARS-CoV-2, aged < 18 y, from France, United Kingdom, United States, Brazil, Argentina, India, Peru, and Saudi Arabia	Neuroimaging showed an immune-mediated parainfectious pattern of disease, which involved the brain, spine, cranial nerves, and nerve roots in 28 children. The most common imaging patterns involved post-infectious immune-mediated acute disseminated encephalomyelitis-like changes of the brain (16 patients), myelitis (8 patients), and neural enhancement (13 patients). Splenial lesions (7 patients) and myositis (4 patients) were predominantly observed in children with MIS.	
Pouletty et al (2020) <sup>38</sup>	MIS-C	16 children, girls:boys ratio of 1:1, median age of 10 y, France	Neurologic symptoms involving headache and meningism were reported in 56% of cases.	
Toubiana et al (2020) <sup>49</sup>	Kawasaki-like MIS	21 children, median age of 7.9 y, France	The study reported irritability to be a common symptom (57%), and 6 (29%) patients presented with headaches, confusion, or meningeal irritation.	
Chiotos et al (2020) <sup>40</sup>	MIS-C	6 children, median age of 8.5 y	Headache, meningism, and altered mentality were observed.	
Verdoni et al (2020) <sup>43</sup>	Kawasaki-like disease	10 children, median age of 7.5 y, Italy	Meningism was observed in 40% of the subjects.	
Dufort et al (2020) <sup>39</sup>	MIS-C	99 children and adolescents; aged 0–5 y: 31%, 6–12 y: 42%, 13–20 y: 26%; United States	Neurologic involvement was reported in 30% of cases.	
Belhadjer et al (2020) <sup>34</sup>	MIS-C	31 children, median age of 10 y, France and Switzerland	Meningism was reported in 31% of cases.	
Feldstein et al (2020) <sup>37</sup>	MIS-C	186 children and adolescents, United States	Neurologic involvement was observed in 5%–11% cases, which included encephalitis, seizures, or mental status alteration.	
Whittaker et al (2020) <sup>47</sup>	MIS-C	58 children, United Kingdom	Headache was reported in 26% of patients.	
Abdel-Mannan et al (2020) <sup>36</sup>	MIS-C	50 children, United Kingdom	MIS-C in 27 children. Among these, 14% showed neurologic symptoms, including encephalopathy, headache, brain stem signs with dysarthria or dysphagia, meningism, and cerebellar ataxia. Peripheral nervous system involvement was seen in all patients, with global proximal muscle weakness and reduced reflexes.	
Abel et al (2020) <sup>44</sup>	MIS-C	1 child aged 2 y	Altered mental health status was observed in the patient. The patient developed reversible encephalopathy.	
LaRovere et al (2021) <sup>27</sup>	Neuropsychiatric	1,695 patients, median age of 9.1 years, United States	Of the patients, 22% presented neurologic involvement. Among these, 322 (88%) had transient symptoms and survived, and 43 (12%) developed life-threatening conditions clinically adjudicated to be associated with COVID-19, including severe encephalopathy, stroke, CNS infection/ demyelination, Guillain-Barré syndrome/variants, and acute fulminant cerebral edema.	
Roussel et al (2021) <sup>50</sup>	Cranial polyneuropathy	6-year-old child, France	First case to report incidence of cranial polyneuropathy in a child infected with SARS-CoV-2.	
Manji et al (2020) <sup>48</sup>	Progressive paresis, bilateral facial nerve paresis	12-year-old boy, Tanzania	First case of acute post-infectious flaccid paralysis, known as Guillain- Barré syndrome, in a boy infected with SARS-CoV-2 in Tanzania.	

Abbreviations: CNS = central nervous system, MIS-C = multisystem inflammatory syndrome in children, OCD = obsessive-compulsive disorder, PANS = pediatric acute onset neuropsychiatric syndrome, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

#### Gupta et al **It is illegal to post this copyrighted PDF on any website.** larger studies with a more robust design to fill data gaps attention of clinicians and researchers.<sup>25</sup> The first few

during the initial wave.

Table 1 presents salient features of studies included in the review. Most studies included participants from the United States (6) and the United Kingdom (4). Three studies were from France, while 2 were from Italy. Inflammatory disorders post-SARS-CoV-2 infection, namely a multisystem inflammatory syndrome in children (MIS-C) and Kawasakilike disease, were reported the most among the studies. The former was reported in 8 articles, 34, 36-40, 44, 47 while 2<sup>43,49</sup> reported the latter. Neuropsychiatric complications were reported in 5,<sup>25-28,30</sup> while 3 articles<sup>29,48,50</sup> described neurologic disorders. Table 2 provides an overview of the newer studies, which include cohort studies from Denmark<sup>51</sup> and the United Kingdom.53,54 An Italian cross-sectional study<sup>52</sup> and Norwegian national register-based cohort study<sup>55</sup> provided patterns of symptomatology, duration of illness, and overall burden on health care.

#### DISCUSSION

In adults, there are reports of marked variability in neuropsychiatric symptoms post–SARS-CoV-2.<sup>11–16</sup> For example, in a Chinese case series<sup>19</sup> of 214 inpatients, neurologic symptoms of stroke, encephalopathy, and myopathy were reported in about one-third of the sample. Also, a French study<sup>20</sup> of 58 COVID-19–positive patients reported neuropsychiatric long COVID symptoms in 33% of the sample. Similarly, an increased prevalence of depression (29%) was reported in another Chinese cross-sectional study<sup>14</sup> of 205 patients. However, another study<sup>21</sup> reported neuropsychiatric manifestations in ~22% of 40,469 patients, with a higher prevalence of headache, sleep disorders, encephalopathy, stroke, transient ischemic attack, seizures, anxiety, mood disorders, and suicidal ideation.

A US-based study<sup>22</sup> reported neurologic or psychiatric diagnosis in 33.62% of 236,379 subjects in the following period of 6 months. The authors<sup>22</sup> reported a similar pattern of a wide range of symptoms, with intracranial hemorrhage, ischemic stroke, parkinsonism, dementia, anxiety disorder, and psychotic disorder the most common. In another study from the United States,<sup>23</sup> the same researchers assessed electronic health records of 44,779 patients with COVID-19 and reported an 18% probability of the first diagnosis of psychiatric illness, including anxiety disorders, insomnia, and dementia, during a period of 14–90 days post–SARS-CoV-2 infection. These trends were suggestive of highly variable symptoms with unaccounted impairments in global functioning.

#### Neuropsychiatric Manifestations of COVID-19 in Children and Adolescents

Toward the end of December 2020, many children did not completely recover from SARS-CoV-2 infection.<sup>3,24</sup> There was increased utilization of online medical forums wherein parents were seeking medical expertise for prolonged clinical manifestations post–COVID-19, which was bought to the

reports include a case series of 5 children with prolonged headaches, difficulty concentrating, brain fog, and memory loss.<sup>26</sup> Buonsenso et al<sup>25</sup> assessed 510 children and reported the presence of lack of concentration (60.6%); difficulty in remembering information (45.9%), performing daily activities (40%), and processing information (32.7%); and short-term memory issues. In another case series of 1,695 patients,<sup>27</sup> neurologic symptoms were reported in 22% of patients, of which 88% presented transient symptoms. The remaining 12% developed life-threatening conditions, like Guillain-Barré syndrome (GBS), encephalopathy, demyelination of CNS, stroke, and acute fulminant edema, which were associated with COVID-19. Among the patients with life-threatening neurologic conditions, 40% presented new neurologic deficits at the time of hospital discharge, whereas 26% died.<sup>27</sup> Another case<sup>28</sup> reported acute-onset neuropsychiatric syndrome post-SARS-CoV-2 infection in 2 children aged 12 and 13 years. The first presented obsessive-compulsive disorder (OCD) symptoms, emotional lability, facial motor tics, and lack of attention 2 months post-infection, and the second presented symptoms of aggressiveness, irritability, inattentiveness, inappetence, facial motor tic, guttural vocal tics, and hyperactivity.<sup>28</sup> A French study<sup>29</sup> of 5 infants reported neurologic symptoms of axial hypotonia or drowsiness and moaning sounds. In a cross-cultural multicenter study, Lindan et al<sup>30</sup> assessed 38 neurologic findings associated with SARS-CoV-2 from France, the United Kingdom, the United States, Brazil, Argentina, Peru, India, and Saudi Arabia. The neuroimaging study's findings were associated with post-infectious immune-mediated acute disseminated encephalomyelitis-like changes of the brain, myelitis, and neural enhancement.<sup>30</sup> A prospective study<sup>31</sup> of 90 children assessed at a median of 112 days post-SARS-CoV-2 infection found 60% of symptoms were associated with functional impairment at 1-7 months.

The COVID-19 pandemic is also associated with MIS-C, which shares common characteristics with Kawasaki disease.32 MIS-C33 associated with COVID-19 presented with toxic shock-like symptoms, hypoxia-ischemia, elevation of inflammatory markers, and increased incidence of end-organ damage, including the heart,<sup>34</sup> kidneys, and other organs.<sup>35</sup> Most of these patients were treated with intravenous immunoglobulin (IVIG) or steroids, the recommended interventions for Kawasaki disease. Most patients either fully recovered or showed considerable improvement after treatment. Neurologic involvement was also reported in approximately 35% of cases.<sup>33,39</sup> Among neurologic symptoms, headaches, meningism, confusion, seizures, muscular weakness, encephalopathy, short-term memory, agitation, and altered mental health status were most common.<sup>36</sup> Several single case studies also reported incidences of MIS-C, wherein some rare neurologic manifestations<sup>37-47</sup> including acute cerebrovascular accidents, reversible splenial lesions, GBS,<sup>48</sup> benign intracranial hypertension, meningoencephalitis,49

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Study	Symptoms or Measures	Study Characteristics	Key Findings
Borch et al (2022) <sup>51</sup>	Both physical and neuropsychiatric symptoms were reported.	Cohort study of 37,522 children in Denmark	Long COVID is rare and of short duration, which resolves within 1–5 mo.
Buonsenso et al (2021) <sup>52</sup>	A mixed range of physical and neuropsychiatric symptoms; insomnia (18.6%) and respiratory symptoms were most common.	A cross-sectional study of 129 children in Italy, assessed 162.5±113.7 days after infection	Of the patients, 42.6% presented at least 1 symptom after 2 months post-infection. Asymptomatic children also developed chronic symptoms.
Stephenson et al (2022) <sup>53</sup>	There are multiple and varied symptom clusters that require multidisciplinary approaches.	A UK cohort study of patients aged 11–17 y from the public health database	Patients who were SARS-CoV-2 positive had similar long COVID symptoms as those who tested negative. Mental health and physical symptoms have relationships.
Molteni et al (2021) <sup>54</sup>	A mixed range of physical and neuropsychiatric symptoms with fatigue and headaches are the most common symptoms.	A UK-based prospective cohort study of patients aged 5–17 y	Long COVID usually had a short duration, but some may have prolonged illness. Most recovered in 56 days and even those who tested negative had persistent illness with impairments.
Magnusson et al (2022) <sup>55</sup>	The overall burden on the health care services in Norway was minimal, and most needed services due to respiratory symptoms.	A national register- based cohort study from Norway of 700,000 children aged 1–19 y	Preschoolers aged 1–5 y took longer to recover (3–6 months) compared to older children (1–3 months).

autoimmune encephalitis, acute disseminated encephalomyelitis, cranial nerve palsies,<sup>50</sup> increased intracranial pressure,<sup>45</sup> and transverse myelitis were recorded in addition to the commonly reported symptoms.

#### Underlying Mechanisms Responsible for the Neuropsychiatric Outcomes of COVID-19

The underlying cellular and molecular mechanisms attributing to the neuroinvasiveness and neurovirulence of SARS-CoV-2 remain poorly understood. Several theories include the direct neurotropism or neuroinvasive potential of SARS-CoV-2. It may also be a consequence of a systemic inflammatory response triggered by the viral infection. Additionally, vascular and prothrombotic effects of SARS-CoV-2 on the CNS or peripheral nervous system vasculature might act as a contributing factor. Lastly, immune-mediated para-infectious or post-infectious autoimmune effect post-SARS-CoV-2 might play an important role.<sup>46</sup> Knowledge of the underlying mechanisms associated with neurologic manifestations of COVID-19 is critical for the development of safe and effective therapeutics. Amid the absence of data and serious limitations in the current body of research, the findings in adults point toward a significant unaccounted impact on the development and health of children.<sup>17</sup>

## Emerging Research, Challenges, and Limitations of Understanding These Findings

At the beginning of the COVID-19 pandemic, parents and clinicians were unclear about the clinical symptomatology and when to seek medical help. However, the increasing global burden of COVID-19 and the presence of delayed neuropsychiatric symptoms has highlighted the potential for a serious public health crisis among children and adolescents. Altogether, these studies highlight the importance of monitoring prolonged neuropsychiatric manifestations in this population.

Recent studies have recognized the challenges in distinguishing long-term symptoms caused by SARS-CoV-2 infection from pandemic-related symptoms. A Danish study<sup>51</sup> reported that the long COVID symptoms could not be attributed to the indirect psychological effects of social isolation, but most cases resolve within 1-5 months. An Italian cross-sectional study<sup>52</sup> of 129 children who tested positive for SARS-CoV-2 infection found that about 43% experienced at least 1 symptom more than 60 days after their initial infection. The common symptoms were fatigue, muscle and joint pain, headache, insomnia, respiratory problems, and palpitations. A striking and unexpected finding was with asymptomatic or mildly symptomatic children who also developed chronic, persisting symptoms. There are limitations to these results<sup>52</sup> given the crosssectional design of the study and relatively short follow-up period, but they underscore the lack of any clear pattern in these symptoms.

One large cohort study<sup>53</sup> in the United Kingdom (CLoCk Study) found that symptoms were reported equally by children who tested positive and who tested negative for COVID-19. Therefore, multidisciplinary approaches were recommended given both physical and mental health symptoms presented concurrently. The calls for holistic approaches for long COVID have been echoed by another UK cohort study,<sup>54</sup> as most patients recovered in 56 days. A linked study<sup>55</sup> of nationwide register data from Norway in 1.3 million children and adolescents found that those aged

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is illegal to post this copy years utilized primary health care services for a longer period after COVID-19 without increasing burden on health care delivery. The most common symptoms were fatigue and dyspnea with a slight male predominance, and symptoms were more often observed in older children, possibly due to better language abilities.<sup>55</sup> The pattern of long COVID is of remitting and relapsing nature.<sup>13</sup>

There are also many methodological issues within the lower level of supporting evidence. The clinical presentations have marked inter-subject variability; therefore, it is difficult to account for the heterogeneity. Respondent bias is likely since symptoms are reported by the parents or caregivers. There are also concerns about underreporting due to the highly overlapping nature<sup>56</sup> of clinical symptomatology. The relapsing and remitting clinical course of SARS-CoV-2 has not been reported or accounted for, which affects the true estimates of long COVID.57 In addition, not having a control group in the studies of children with other illnesses or infections may affect overall results. Finally, the US Centers for Disease Control and Prevention is not tracking mild COVID-19 breakthrough illnesses and so might miss many cases that lead to long COVID.58

#### Interventions: Prevention, Accommodations, and Treatment Strategies

Researchers have utilized the best available evidence using a modified Delphi process to define long COVID in children as an illness that "occurs in young people with a history of confirmed SARS-CoV-2 infection, with at least one persisting physical symptom for a minimum duration of 12 weeks after initial testing that cannot be explained by an alternative diagnosis."59(p11) And, interestingly, waxing and waning of symptoms is more widely accepted.<sup>60</sup>

Long COVID is now a disability under the Americans with Disabilities Act, Section 504, and Section 1557.<sup>61</sup> Given the serious nature of these impairments and their overall impact on the functioning of children, the US Department of Education's Office for Civil Rights and Office of Special Education and Rehabilitative Services has also recognized long COVID as a disability. It comes under 2 Federal laws, Section 504 of the Rehabilitation Act of 1973 (Section

**chted PDF on any websit** 504) and Parts B and C of the Individuals with Disabi Education Act.62

There are reports of a surge in the COVID-19 rehabilitation clinics and specialist services across various tertiary centers in the United States. The number of patients seeking medical care has increased exponentially since the Delta and Omicron variants emerged.<sup>63</sup> In the United Kingdom, there are reportedly 80 clinics run by the National Health Service to treat long COVID-related symptoms with multidisciplinary approaches for both adults and children.<sup>64</sup>

The experts have called for widespread vaccination as a preventive measure to contain the burden of long COVID in children. UK government data suggest a 13% decrease in self-reported symptoms among those who already had long COVID after the first dose and a further 9% reduction after the second dose.<sup>65</sup> In 2021, the US Congress allocated the National Institutes of Health (NIH) \$1.15 billion over 4 years to study the long-term health consequences of SARS-CoV-2 infection. The NIH granted the first awards for a long COVID research program called RECOVER, which will collect data on vaccinated children and adolescentsthe missing information from current studies.<sup>66</sup> These are steps in the right direction to address the knowledge gap and critical issues in the methodology of the research evidence.

#### CONCLUSION

Long COVID or post-SARS-CoV-2 neuropsychiatric manifestations are widely accepted in adults, and emerging evidence supports its presence in child and adolescent populations. With the emergence of new variants and higher rates of infection among children and adolescents, there is a gap in the information about the true estimates of long COVID. Knowledge of the trends of overall duration, pathophysiology, risk factors, and impairments in social and academic areas is critical to understanding the burden of long COVID in children and adolescents. The role of clinical monitoring with multidisciplinary approaches for physical problems, reasonable academic accommodations, preventive vaccinations, and mental health support are a few strategies to consider amid this rapidly evolving issue.

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### POSTTEST

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- I. Miguel, an 8-year-old boy who has been adopted from Guatemala, presents to your office for a follow-up visit after testing positive for COVID-19 3 weeks ago. His 2-year-old sister, Betsy, who lives in the same household, also experienced symptoms but tested negative for the virus. The concerned parents ask for information about the risk factors, prognosis, and preventive measures for long COVID in children and adolescents. Which of the following statements would you communicate to Miguel's and Betsy's parents regarding their concerns?
  - a. Long COVID symptoms vary across cultures.
  - b. In children and adolescents who either tested positive or negative for COVID-19, long COVID manifests equally, but the symptoms are significantly different.
  - c. Vaccination may play a role in prevention of long COVID in children and adolescents.
  - d. In most cases, children and adolescents will recover within 6 weeks with no residual impairment.
- 2. Which of the following conditions post-SARS-CoV-2 infection were reported the most among the studies included in the review article?
  - a. Obsessive-compulsive disorder
  - b. Meningoencephalitis
  - c. A multisystem inflammatory syndrome
  - d. Meningitis
- 3. A recent Norwegian study based on national register data found that long COVID is more common in older children due to which of the following reasons?
  - a. COVID-19 is less likely to infect younger children.
  - b. In younger children, the symptoms are less severe, so they are less likely to be reported.
  - c. Older children have better language abilities.
  - d. Compared to younger children, older children exhibited more physical symptoms like dyspnea, making diagnosis easier.