



# Neurocognitive Deficits Associated with COVID Infection and Long COVID in Children and Adolescents



Christine Koterba, PhD, ABPP  
Pediatric Neuropsychologist

Kristen R. Hoskinson, PhD  
Pediatric Neuropsychologist

 NATIONWIDE CHILDREN'S  
The world's best & most caring children's hospital.

1

---

---

---

---


---

---


---


---

## Questions?



Type in the question box during the presentation or at the end!



 NATIONWIDE CHILDREN'S  
The world's best & most caring children's hospital.

2

---

---

---

---


---


---

---

---

## Outline

-  COVID-19 and Long COVID in Kids
  - COVID-19/MIS-C
  - Long COVID
  - Cultural Considerations
- Neurological Impact of COVID
  - Acute Infection/MIS-C
  - Long COVID
- Neuropsychological Impact of COVID in Kids
  - Neuropsychological Findings
  - Proposed Battery
  - Recommendations

 NATIONWIDE CHILDREN'S  
The world's best & most caring children's hospital.

3

---

---

---

---

---

---

---

---

**SARS-CoV-2**

- The corona virus responsible for the COVID-19 pandemic.

**COVID-19 infection**

- The disease state associated with the invasion and growth of SARS-CoV-2 variants in the human body.

**Neuropsychiatric-PASC syndrome**


- Cognitive and behavioral symptoms arising after COVID-19 infection, lasting at least 2 months, due to direct or indirect mechanisms injuring or disrupting brain functions.

**Neuropsychological-PCC**

- Cognitive and behavioral symptoms arising and persisting 4+ weeks after COVID-19 infection, due to brain injury/disruption (i.e., Neuropsychiatric-PASC), psychological reaction to infection and pandemic, or other unclear mechanism.

**Long-COVID**

- Less specific term often preferred by patient advocates and families.



4

---

---

---

---

---

---

---

---


---

---

## COVID-19 in Kids

*Pediatric cases (American Academy of Pediatrics)*

- Children under 20 make up around ~19% of reported cases
- 15.5 million children reported since the start of the pandemic
- Acute illness → hospitalization rates between 0.1-2%; mortality ~0.03-0.07% (much lower compared to adults/elderly)
- Most children have mild (or no) symptoms and recover fully
- But...a small group develops severe COVID-19
  - MIS-C
  - COVID and severe illness and hospitalization
  - Long COVID



5

---

---

---

---

---

---

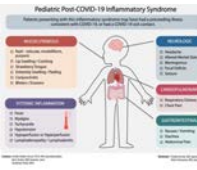
---

---

---

---

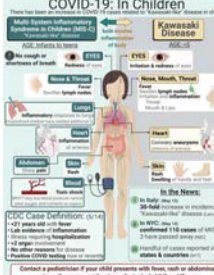
**Pediatric Post-COVID-19 Inflammatory Syndrome**

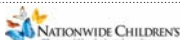


**Multisystem inflammatory syndrome in children (MIS-C)**

- Children with fever
- Inflammation
- Severe illness → hospitalization
- At least 2 organ systems
- Symptoms vary
- COVID exposure/no other alternative
- More common in school aged children, males, and certain ethnicities

**COVID-19: In Children**





6

---

---

---

---

---

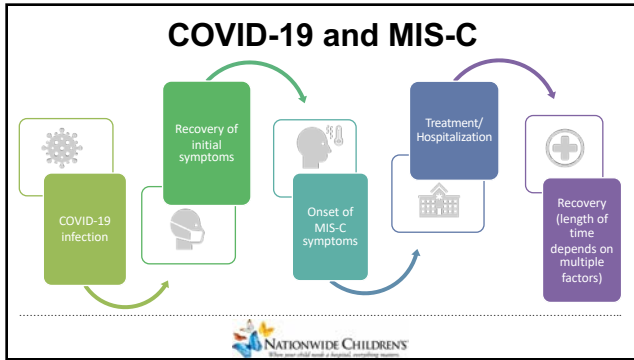
---

---

---

---

---



7

---

---

---

---

---

---

---

---

### Important Points

---

Vast majority of children recover, but some require weeks of treatment and intensive care

---

Impact for children may be significant because of periods of neurodevelopment

---

Early identification, diagnosis, and effective treatment are critical (IVIG, steroids, etc.)

---

Outcomes are still largely unknown

---

**NATIONWIDE CHILDRENS**  
The world's first and largest pediatric hospital

8

---

---

---

---

---

---

---

---

### Long COVID

- Post COVID-19 Condition (WHO consensus study)
  - History of probable or confirmed SARS-CoV-2 infection
  - 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis
- Common symptoms = fatigue, shortness of breath, cognitive dysfunction, and others
- Impact everyday functioning
- Symptoms may be new onset, following initial recovery, or persist from the initial illness
- Symptoms may fluctuate or relapse
- \*Separate definition may be applicable for children

**NATIONWIDE CHILDRENS**  
The world's first and largest pediatric hospital

9

---

---

---

---

---

---

---


---

### Long COVID in Kids

**Research is mixed**

- Early reports: 25-58% of children with PCCS
- Molteni et al., 2021: 4% of hospitalized children with PCCS at 28 days; 2% at 56 days
- Some studies have not found differences in rates of children with a history of SARS-CoV-2 and controls

Lots of limitations in previous studies (lack of control group, biased sample, etc.)



10

---

---

---

---

---

---

---

---

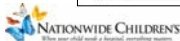
### Long COVID in Kids: Review

REVIEW ARTICLES 2021

How Common is Long COVID in Children and Adolescents?  
*Petra Zimmermann, MD, PhD,\*†‡; Laura F. Pittet, MD-PhD,§¶ and Nigel Curtis, FRCPCH, PhD||*

The Pediatric Infectious Disease Journal 2022

The Challenge of Studying Long COVID: An Updated Review  
*Zimmermann, Pittet, Molteni, Luan, & Curtis, 2022*



11

---

---

---

---

---

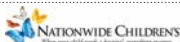
---

---

---

### Long COVID in Kids: Review

2021	2022
<ul style="list-style-type: none"> <li>14 studies</li> <li>5 with control groups</li> <li>Rates: 4-66%</li> </ul>	<ul style="list-style-type: none"> <li>27 studies</li> <li>9 with control groups</li> <li>Rates: &lt;4%-58%</li> </ul>



12

---

---

---

---

---

---

---



---

### Long COVID in Kids: Review Findings

Rates of long COVID varies significantly

Common symptoms varied

- Headache
- Fatigue
- Sleep disturbance
- Abdominal pain
- Myalgia
- Congested/runny nose
- Cough
- Chest pain/tightness
- Disturbed smell

13

---

---

---

---

---

---


---

---

### Long COVID in Kids: Review Findings

Significant limitations make it hard to interpret the findings

- Hard to distinguish between COVID and pandemic related issues
  - Lockdown measures
  - Social isolation
  - Virtual school
  - Pandemic related stress (illness and deaths of loved ones)
- Psychosomatic and physical symptoms are higher in ALL children



14

---

---

---

---

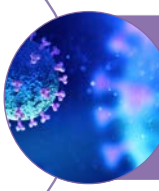
---

---

---

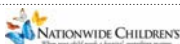
---

### Long COVID in Kids: Review



Limitations

- Lack of clear definition
- Variable follow-up
- Self or parent reported symptoms only
- Differing symptom measures
- Hard to find an appropriate control group
- Response bias



15

---

---

---

---

---

---

---

---

### Long COVID in Kids: What do we actually know?

Research is mixed, likely because of heterogeneity and limitations

Long COVID symptoms may have an impact...but the pandemic also has a significant impact on kids (and all of us!)

Psychosocial follow-up and neurodevelopmental monitoring is important, especially for high-risk groups



16

---

---

---

---

---

---

---

---

### What about the effect of the pandemic??

Increase in mortality from non-COVID causes (widespread disruption in healthcare)

Increased poverty rates

Lockdown measures and limited access to remote learning, socialization, work, etc.

80 million children under 18 without routine vaccinations

Stress related to uncertainty about the future, loss of loved ones, illness, etc.

Reduction in in-person learning has likely impacted academic gains

Over half of children report physical and psychological symptoms

**STRESS**



17

---

---

---

---

---

---

---

---

### COVID-19 Cultural Considerations

Figure 1  
Cumulative COVID-19 Age-Adjusted Infection Rates by Race/Ethnicity, 2020-2022

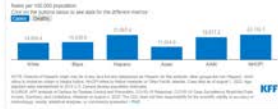
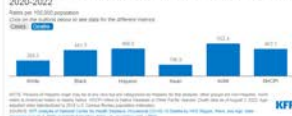


Figure 2  
Cumulative COVID-19 Age-Adjusted Mortality Rates by Race/Ethnicity, 2020-2022



Kaiser Family Foundation  
<https://www.kff.org/coronavirus-covid-19/issue-brief/covid-19-cases-and-deaths-by-race-ethnicity-current-data-and-changes-over-time/>



18

---

---

---

---

---

---

---

---

## COVID-19 Cultural Considerations

- Population-based study
- Race-specific disparities
  - Positive test results
  - Hospital contact
  - Hospital admission
  - Hospitalization duration
  - ICU admission
- Important implications for public health and policy

**Figure 1. Manually Adjusted Regression Analysis Exploring the Association Between Race and Outcomes of Interest**

Outcome	Race	Adjusted OR	95% CI
Positive test result	White	1.00	
	Black	1.20	1.05-1.37
	Hispanic	1.15	1.00-1.33
Hospital contact	White	1.00	
	Black	1.30	1.10-1.55
	Hispanic	1.25	1.05-1.50
Hospital admission	White	1.00	
	Black	1.40	1.20-1.65
	Hispanic	1.35	1.15-1.60
Hospitalization duration	White	1.00	
	Black	1.50	1.30-1.75
	Hispanic	1.45	1.25-1.70
ICU admission	White	1.00	
	Black	1.60	1.40-1.85
	Hispanic	1.55	1.35-1.80

Saatci et al., 2021

19

---

---

---

---

---

---

---

---

## Outline

**COVID-19 and Long COVID in Kids**

**Neurological Impact of COVID in Kids**

**Neuropsychological Impact of COVID in Kids**

- COVID-19
- Complicated COVID
- Cultural Considerations

- What do we know?
- What don't we know?
- Neurodevelopmental Considerations

- Neuropsychological Findings
- Case Example
- Recommendations

20

---

---

---

---

---

---

---

---

## COVID-19 and Neurological Impact

- Studies of the neurological impact of acute COVID-19 infection are rapidly evolving
- Around 1% may have neurological involvement
  - Can be mild or severe
  - Can include non-specific symptoms or more severe impact
  - Rates in those with more severe infection (e.g., MIS-C) are considerably higher, ~20-35%

21

---

---

---

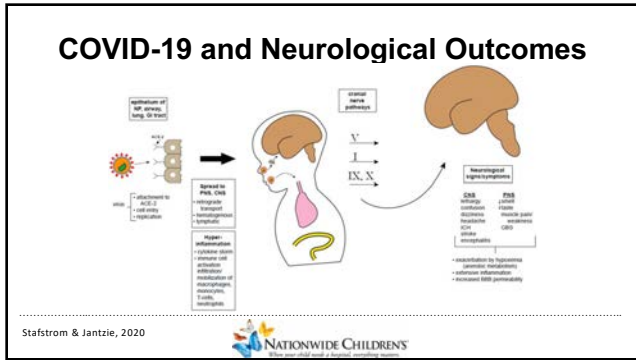
---

---

---

---

---



22

---

---

---

---

---

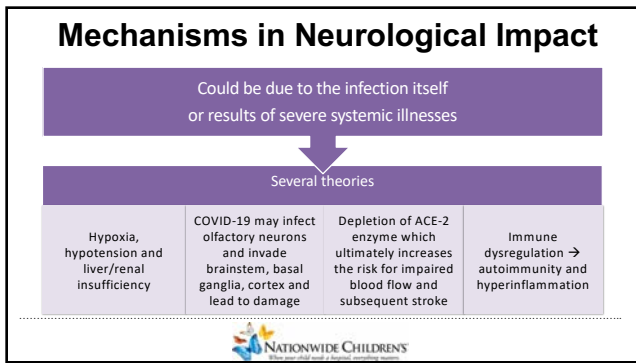
---

---

---

---

---



23

---

---

---

---

---

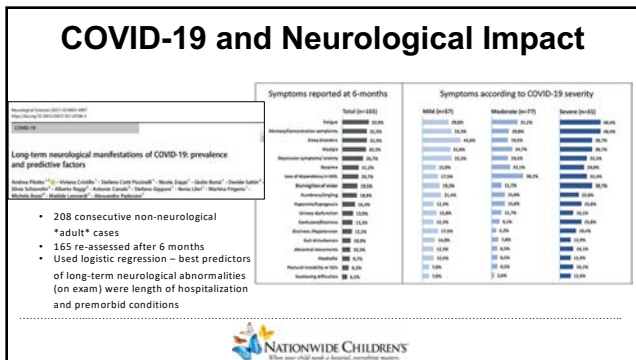
---

---

---

---

---



24

---

---

---

---

---

---

---

---

---

---



## COVID-19 and Neurological Outcomes

**Neurologic Features Associated With SARS-CoV-2 Infection in Children: A Case Series Report**

*Journal of Child Neurology* 2020

Francisca Sandoval, MD<sup>1</sup>, Katherine Jahn, MD<sup>2</sup>, Gerardo Miroles, MD<sup>3</sup>, Carolina Valdivia, MD<sup>4</sup>, Alejandra C. Echeverri, MD<sup>5</sup>, Maria José Fernández, MD<sup>6</sup>, N. María Saez, MD<sup>7</sup>, Gonzalo Barrera, MD<sup>8</sup>, Cecilia Páez, MD<sup>9</sup>, Marcela Alborn, MD<sup>10</sup>, Fernando Sarmiento, MD<sup>11</sup>, Pía Quinteros-Rico, MD<sup>12</sup>, Carlos Robles, MD<sup>13</sup>, and Giovanni Topfer, MD<sup>14</sup>

- Review of patients with COVID-19 seen at hospital in Chile
- 90 total patients
- 13 patients with new-onset neurologic manifestations associated with COVID-19 infection
- 4 patients showed exacerbation of epilepsy

**Figure 3. Neurologic manifestations, ages and symptoms. \*Other than MIS-C and Hospitalized.**

*Most relevant: encephalopathy, seizures, muscle weakness*  
*Neurologic sx were more common in MIS-C and resolved when systemic illness resolved*

**NATIONWIDE CHILDREN'S**  
The world's first and largest pediatric system

25

---

---

---

---

---

---

---

---

---

---

## Neurological Outcomes

Can range from mild (neuromotor deficits) to severe (cognitive impairment)

May not initially be apparent and may appear over time with increasing demands as children age

Even mild difficulties can have a huge impact on a child's functioning

**NATIONWIDE CHILDREN'S**  
The world's first and largest pediatric system

26

---

---

---

---

---

---

---

---

---

---

## COVID-19 and Neurological Involvement

3 "at-risk" groups for severe COVID-19 and neurological impact

- Children with underlying medical conditions
- Younger children (infants and toddlers)
- Children who develop multisystem inflammatory syndrome in children (MIS-C)

**NATIONWIDE CHILDREN'S**  
The world's first and largest pediatric system

27

---

---

---

---

---

---


---

---


---

---


## MIS-C and Severe Neurological Impact



20-35% of children with MIS-C may have more severe neurological involvement



MIS-C and cerebrovascular disease → more microvascular infarcts in deep brain structures (compared to those without MIS-C)

 **NATIONWIDE CHILDREN'S**  
The world's best & most innovative children's hospital

28

---

---

---

---

---

---

---

---

---

---

## COVID-19 and Neurological Impact

6-month multidisciplinary follow-up and outcomes of patients with pediatric inflammatory multisystem syndrome (PIMS-TS) at a US tertiary pediatric hospital: a retrospective cohort study

Lancet Child Adolesc Health 2021

- 46 youth with MIS-C
- **52%** still had abnormal neurological exam at 6 weeks, and **39%** at 6 months

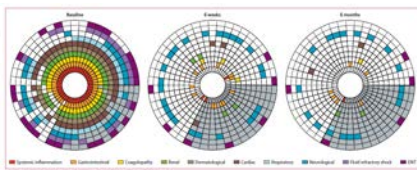



Figure 3 System involvement at baseline (A), 6 weeks (B), and 6 months (C)  
The circular diagrams are divided into 12 system categories (legend) and are presented for each time point across the three timepoints. Systemic inflammation refers to fever, malaise, fatigue, or tachycardia; Gastrointestinal involvement refers to abdominal pain, vomiting, diarrhea, or abnormal stool; Cardiac involvement refers to abnormal ECG, or evidence of abnormal echocardiography; Neurological involvement refers to abnormal or any neurological examination; Renal involvement refers to abnormal serum creatinine; Hematological involvement refers to abnormal hemoglobin; Skin/soft tissue involvement refers to any abnormal skin findings. Legend: Systemic inflammatory (red), Gastrointestinal (orange), Cardiac (yellow), Neurological (green), Hematological (blue), Renal (purple), Hematological (brown), Neurological (pink), and Skin/soft tissue (grey).

 **NATIONWIDE CHILDREN'S**  
The world's best & most innovative children's hospital

29

---

---

---

---

---

---

---

---

---

---

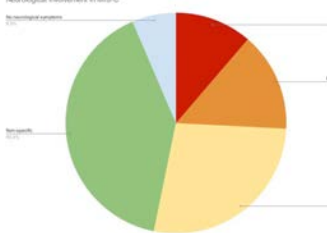
## MIS-C and Neurological Outcomes


**Neurological Involvement in Multisystem Inflammatory Syndrome in Children: Clinical, Electroencephalographic and Magnetic Resonance Imaging Peculiarities and Therapeutic Implications. An Italian Single-Center Experience**

Frontiers in Pediatrics 2022

- Most research on neurological changes focuses on severe COVID-19 infection, particularly MIS-C
- Bova et al., August 2022 – retrospective analysis of 62 children with MIS-C hospitalized between October 2020 and March 2022. *Frontiers in Pediatrics*

Neurological involvement in MIS-C



 **NATIONWIDE CHILDREN'S**  
The world's best & most innovative children's hospital

30

---

---

---

---

---

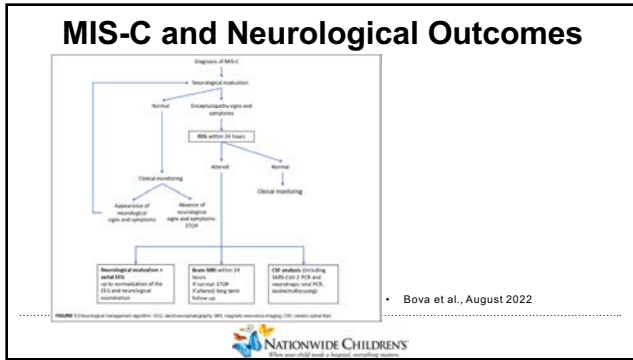
---

---

---

---

---



31

---

---

---

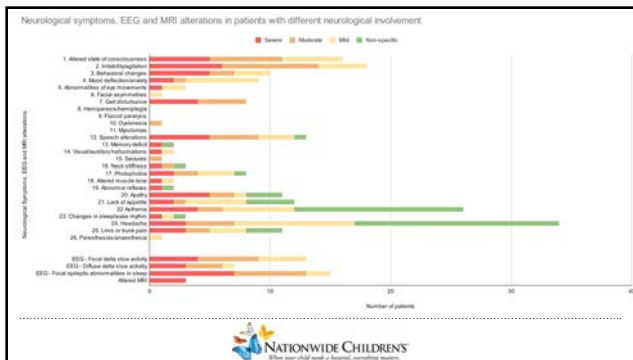
---

---

---

---

---



32

---

---

---

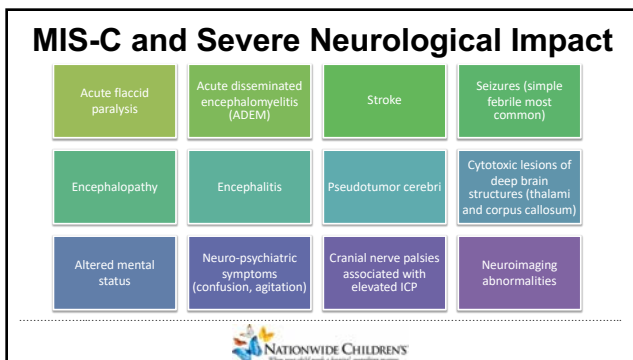
---

---

---

---

---



33

---

---

---

---

---

---

---

---

# “Characteristic” Neuroimaging Features

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)  
 ScienceDirect  
 Biomedical Journal  
 Journal homepage: [www.elsevier.com/locate/bsj](http://www.elsevier.com/locate/bsj)

Review Article: Special Edition  
**Spectrum of neuroimaging mimics in children with COVID-19 infection**

Alex Mun-China Wong <sup>a,b,\*</sup>, Cheng Hong Toh <sup>b,c</sup>

Verdict: MRI features vary greatly and align with neurological symptoms, e.g.:

- ADEM is usually associated with cerebral white matter lesions in addition to subcortical lesions
- Acute necrotizing encephalopathy shows frank thalamic changes
- Vasculitis with infarction will depend on the site of the lesion

This also affects the type of sequences you want to acquire, and location of the images (e.g., spinal MRI for GBS or transverse myelitis)



34

---

---

---

---

---

---

---

---

---

---

Review Article: Special Edition  
**Spectrum of neuroimaging mimics in children with COVID-19 infection**  
 Alex Mun-China Wong <sup>a,b,\*</sup>, Cheng Hong Toh <sup>b,c</sup>

Fig. 2. Encephalitis in a 6-year-old girl presenting with fever, seizure, and coma. Axial (A) T1-weighted and (B) fluid attenuated inversion recovery (FLAIR) and (C) coronal T2-weighted images show abnormal signals in the bilateral frontal, parietal, and temporal regions. Axial diffusion-weighted image reveals decreased diffusion (high signal intensity in the acute regions and mildly decreased diffusion in the thalamus). (D) Axial arterial-spin labeling perfusion image showing global hyperperfusion of the brain. (E) Coronal post-contrast T1-weighted image showing patent bilateral middle cerebral arteries.

35

---

---

---

---

---

---

---

---

---

---

Review Article: Special Edition  
**Spectrum of neuroimaging mimics in children with COVID-19 infection**  
 Alex Mun-China Wong <sup>a,b,\*</sup>, Cheng Hong Toh <sup>b,c</sup>

Fig. 3. Acute necrotizing encephalopathy in a 3-year-and-3-month-old girl presenting with fever, seizure, and conscious disturbance. (A) Axial FLAIR and (B) coronal T2-weighted images show hyperintensities in the bilateral thalami and bilateral frontal deep white matter. (C) Axial T2-weighted image reveals hyperintensities, suggesting hemorrhage in the thalami. (D) Axial diffusion-weighted image showing decreased diffusion in the bilateral thalamic lesions surrounding the hemorrhages. (E) Axial post-contrast T1-weighted image reveals no contrast enhancement of the abnormalities.

36

---

---

---

---

---

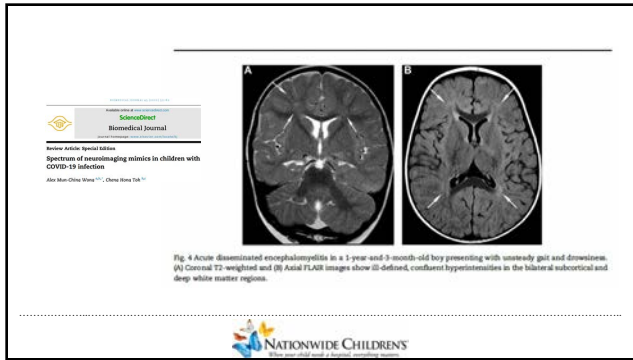
---

---

---

---

---



37

---

---

---

---

---

---

---

---

### Some Good News?

Is it permanent?!

- *Very small number* who have follow up MRI suggest resolution of structural brain abnormality

Lots of limitations in previous studies (lack of control group, biased sample, etc.)

38

---

---

---

---

---

---

---

---

### Acute COVID/MIS-C: What do we know?

Research is mixed, and pediatric literature lags *far* behind adult evidence base

---

A small percentage of kids with COVID-19 have severe neurologic symptoms, and most appear to resolve\*

---

The very few MRI studies suggest particular changes in subcortical gray matter and white matter

\*but, new neurologic symptoms can emerge post-acute recovery...

39

---

---

---

---

---

---

---

---

## Long COVID Mechanisms

### Potential physiological mechanisms

- Cells and tissues controlling blood flow get damaged → tiny blood clots leftover from the virus → disrupt circulation → lingering symptoms (*minute clots*)
- COVID virus lasts in the body and continues to persist in many areas of the body (*lingering virus*)
- Immune system gets out of whack even months after infection (*immune abnormalities*)

Could be a combination of all of these (or something else)



40

---

---

---

---

---

---

---

---

## Long COVID-19 and Neurological Outcomes

**The neurobiology of long COVID**

Monje & Iwasaki, 2022; Neuron



41

---

---

---

---

---

---

---

---

## What the Internet Tells Us: Long COVID and the Brain

**Long COVID has some weird symptoms. Face distortions may be one clue.**

**Even mild Covid is linked to brain damage, scans show**

**Evidence is Mounting That Covid Is B for the Brain**

**Mild COVID Linked to Brain Damage: What That Means for You**

**Long COVID Now Looks like a Neurological Disease, Helping Doctors to Focus Treatments**



42

---

---

---

---

---

---

---

---

### My Reading List: Long COVID and the Brain

The collage features three research articles:

- Neurological Manifestations of Long COVID: A Single-Center One-Year Experience** (Journal of Neurological Disease and Treatment)
- Long COVID-19 in children: an Italian cohort study** (Italian Journal of Pediatrics)
- Long-term follow-up of dynamic brain changes in patients recovered from COVID-19 without neurological manifestations** (Journal of Neurological Disease and Treatment)

The Nationwide Children's Hospital logo is at the bottom.

---

---

---

---

---

---

---

---

43

### Long COVID Literature

Where are we now?

- Growing quickly, though the quality is still inconsistent and we still need to extrapolate from adult literature
- Eclipsing research in MIS-C
- Staying on top of it can be challenging

A quick review...

---

---

---

---

---

---

---

---

44

### Long COVID and Symptom Burden

Neurological Manifestations of Long COVID: A Single-Center One-Year Experience

Caveat:  
103 consecutively referred adults

- It's not just those hospitalized/severely ill with COVID-19
  - 23.3% hospitalized, 3.0% in ICU
- It's not just those with pre-existing neurologic complaints
  - 86.4% of symptoms were new-onset
  - The remaining 13.6% were pre-existing *but exacerbated*

---

---

---

---

---

---

---

---

45

### Long COVID and Symptom Burden

**Neurological Manifestations of Long COVID: A Single-Center One-Year Experience**

**Caveat:**  
103 consecutively referred adults

**Neurological Symptoms**

Symptom	Acute	Persistent
Dizziness	100%	90%
Sensitivity alterations	80%	70%
Sleep disorders	70%	60%
Cognitive disorders	60%	50%
Headache	50%	40%
Olfactory/gustatory dysfunction	40%	30%
Chronic Fatigue	30%	20%

41/103 underwent MRI  
- Over 90% had normal MRI

So, the link between neurologic symptoms and brain structure isn't as clear

**NATIONWIDE CHILDRENS**  
The world's first and best pediatric system

46

---

---

---

---

---

---

---

---

---

---

### Long COVID and the Brain

**Long-term follow-up of dynamic brain changes in patients recovered from COVID-19 without neurological manifestations**

**Caveat:**  
More research in adults

Longitudinal follow up of 50-70yo patients, without neurologic symptoms 10-months post-dx

COVID-19 patients without neurological manifestations - MOSQ

Discharge → 3-month follow-up (MOSQ, MO/SQ+INC) → 6-month follow-up (MRI scans: T1, BRAVO, pCASL, DTI) → 10-month follow-up (MOSQ/SQ)

Longitudinally paired and cross-sectional comparisons

Figure 1. Flow diagram of the experimental design. Flow data sets were acquired in follow-up studies. Green color, relative data, have been published in our former work (45). Blue color, research centers focused in this study. BRAVO, brain volume; DTI, diffusion tensor imaging; MO, mild group at 3 months after discharge; MQ, mild group at 6 months after discharge; MC, normal control; pCASL, perfusion-sensitive arterial spin labeling; SQ, severe group at 3 months after discharge; SCL, severe group at 6 months after discharge.

**NATIONWIDE CHILDRENS**  
The world's first and best pediatric system

47

---

---

---

---

---

---

---

---

---

---

### Long COVID and the Brain

**Long-term follow-up of dynamic brain changes in patients recovered from COVID-19 without neurological manifestations**

**Caveat:**  
More research in adults

Longitudinal follow up of 50-70yo patients, without neurologic symptoms, 10-months post-dx

Significant cortical thickness differences in paired comparisons within MQ and SQ

A MQ2 + MQ1 vs SQ2 + SQ1 (Superior frontal cortex)  
B SQ2 + SQ1 vs SQ1 (Superior frontal cortex)  
C SQ2 + SQ1 vs SQ1 (Superior frontal cortex)

Figure 3. Cortical thickness analysis. A-C) There were only significant differences in paired comparisons. L, left; MQ, mild group at 3 months after discharge; MQ2, mild group at 6 months after discharge; R, right; SQ, severe group at 3 months after discharge; SQ2, severe group at 6 months after discharge.

**NATIONWIDE CHILDRENS**  
The world's first and best pediatric system

48

---

---

---

---

---

---

---

---

---

---



## Long COVID and the Brain: But why?

**Role of Demyelination in the Persistence of Neurological and Mental Impairments after COVID-19**

Manish V. Khanna<sup>1,2,3</sup>, Daria A. Karama<sup>1,2,3</sup> and Anu V. Nair<sup>1,2,3</sup>

One theory: a white-matter hypothesis

Aligns with the higher proportion of subcortical and white matter abnormalities

Figure 3. The schematic representation of the relationship between COVID-19, demyelination, and neurological disorders.

**NATIONWIDE CHILDRENS**  
The world's first and largest pediatric system.

49

---

---

---

---

---

---

---

---

---

---

## Long COVID and the Brain: But why?

**scientific reports**

**OPEN** Long-COVID in children and adolescents: a systematic review and meta-analysis

My opinion: we should view this with some degree of urgency – reminder of the prevalence of long COVID in kids:

*We don't know* the level of impact on developing brains

*We don't know* how much abnormalities resolve over time

*We don't know* how these fill in gaps in neurologic symptoms

Figure 2. The prevalence of long COVID symptoms in children and adolescents. The authors reported the prevalence of long COVID symptoms in children and adolescents. Prevalence was 25.24% (95% CI 19.28–31.20).

**NATIONWIDE CHILDRENS**  
The world's first and largest pediatric system.

50

---

---

---

---

---

---

---

---

---

---

## Outline

**COVID-19 and Long COVID in Kids**

**Neurological Impact of COVID**

**Neurodevelopmental Considerations of COVID**

- COVID-19/MIS-C
- Long COVID
- Cultural Considerations

- Acute Infection/MIS-C
- Long COVID

- Neurodevelopment
- Cognitive Outcomes
- Recommendations

**NATIONWIDE CHILDRENS**  
The world's first and largest pediatric system.

51

---

---

---

---

---

---

---

---

---

---

## Neurodevelopmental Considerations

Neurodevelopmental assessment/surveillance

School and academic development

New things to address in evaluations



52

---

---

---

---

---

---

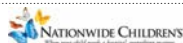
---

---

## Neurodevelopmental Surveillance



- Scoping review of COVID-19 in children
- 31 COVID-19 articles and 21 describing other coronaviruses
  - Guidance for neurodevelopmental monitoring and surveillance



53

---

---

---

---

---

---

---

---

## Neurodevelopmental Surveillance

Scoping review findings

- Evidence of neurological impact associated with almost all coronaviruses in children
- Despite evidence of neurological involvement, little research on long-term neurodevelopmental outcomes/neuropsychological functioning

"Critical gap in knowledge of the long-term effects on child neurodevelopment in these infections"



54

---

---

---

---

---

---

---

---

## Neurodevelopmental Surveillance

**TABLE 4**  
Signs of Potential Neurodevelopmental Impairment Following Acquired Brain Injury

Developmental Domain	0-3 Years Old	3-6 Years Old	6-18 Years Old
<b>Cognitive</b>	Lack of object registration; does not develop pretend play; slower development of self-help skills (e.g., spoon use)	Slower or lack of self-help skills; slower than peers	Needs longer time to process and/or repetitions when learning or completing tasks; forgetfulness (e.g., "not remembering anything"); inattention; executive dysfunction (e.g., poor organization and planning)
<b>Language</b>	Delay in expressive and receptive language milestones (e.g., pointing to identify; novel 2-word sentences; concept of "new")	Does not ask or understand "Why" questions; difficulty with prepositions, word-finding, and/or following instructions	Inconsistent word use or word-finding problems; difficulty with social communication and interactions; struggle with multi-step instructions
<b>Academic</b>	Difficulty learning colors, sorting, matching, counting etc.; does not join in rhyming games	Difficulty learning letters, letter sounds, numbers, counting with one-to-one correspond	Struggling in school; more commonly with reading competencies, written expression, and math
<b>Motor</b>	Delay in gross motor (e.g., walking, jumping) and/or fine motor milestones (e.g., scribbling, drawing lines, or a circle); poor orienter skills (drawing difficulty)	Trouble learning gross motor skills (e.g., hopping on one foot, skipping, riding bicycle); difficulty drawing shapes; shows an immature person for age; struggle with cutting with scissors or other things	More clumsy than peers; poor handwriting; struggles with fine motor skills
<b>Mood/behavior</b>	Excessive or persistent irritability; excessive tantrums; changes in sleep initiation or duration	Emotional dysregulation; hyperactivity and impulsivity; changes in sleep initiation or duration	Emotional dysregulation; hyperactivity and impulsivity; depression or anxiety; changes in sleep initiation or duration

- Ask about the above areas
- If areas of difficulty are identified, consider further follow-up (i.e., neuropsychology)

Singer et al., 2021



55

---

---

---

---

---

---

---

---

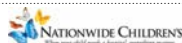
---

---

## Neurodevelopmental Surveillance

Populations to pay special attention to

- Acute flaccid paralysis (any etiology)
- Seizures – status epilepticus
- ADEM
- Encephalitis
- Cerebrovascular disease/stroke
- MIS-C
- Severe systemic illness/PICU admission
- Psychosocial impact
- Stress and trauma of severe illness



56

---

---

---

---

---

---

---

---

---

---

## Neurodevelopmental Surveillance

*“to achieve optimal functional outcomes and quality of life, children who experience severe neurological illness due to coronaviruses, including all those who require intensive care, should receive longitudinal neurodevelopmental monitoring to detect overt and subtle deficits and guide therapy”*  
(Singer et al., 2021)



57

---

---

---

---

---

---

---

---

---

---

### COVID-19 Cognitive Outcomes – Adults Short Term

**EMR review of 236,379 patients**  
Taquet et al. (2021)

High rates of psychiatric diagnoses (e.g., depression, anxiety)

Are high rates directly related to COVID-19 infection?

Are high rates related to experience of significant psychosocial stressors, which includes severe illness?

Higher rates of stroke in patients who were hospitalized

ICU = 6.92%

Encephalopathy/delirium = 9.35%

No hospitalization = 1.33%



58

---

---

---

---

---

---

---

---

### COVID-19 Cognitive Outcomes – Adults Short Term

**3 PMR patients**  
Whiteside et al., (2021)

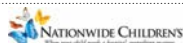
Patients tested 1-2 months after diagnosis

Working memory and executive functioning weaknesses

**29 patients**  
Zhou et al., (2020)

1 measure of sustained attention related to COVID-19

No PVT, memory, or EF testing



59

---

---

---

---

---

---

---

---

### COVID-19 Cognitive Outcomes – Adults Short Term

**Medically stable inpatients**  
Jaywant et al., (2021)

Attention and executive functioning weaknesses

40% reported psychiatric symptoms (anxiety, depression)

**Hospitalized patients with severe COVID-19**  
Almeira et al., (2020);

Evidence of disruption in memory, attention, executive functions



60

---

---

---

---

---

---

---

---

### COVID-19 Cognitive Outcomes – Adults Long Term

Soraas et al., (2021)	High incidence of self-reported memory complaints No objective testing
Hampshire et al., (2021)	Cognitive deficits based on 1 online test No controls or PVT
Becker et al., (2021)	Executive functioning, processing speed, encoding, retrieval deficits 7.6 months after diagnosis No PVT



61

---

---

---

---

---

---

---

---

### Long COVID-19 Cognitive Outcomes – Adults

COVID-19 Articles

**Outcomes in post-acute sequelae of COVID-19 (PASC) at 6 months post-infection Part 1: Cognitive functioning**

Douglas M. Whitehead, Michael R. Eason, Savana M. Niemi, James Porter, Erin Holman, Eric J. Walbrun, et al.

Pages 824-829 | November

- Large battery of tests
- Very few scores in impaired range (>2 SD below mean)
- Some scores in the borderline performance range (1-2 SDs below mean)
- Elevated mood symptoms
- Correlation between cognition and mood/anxiety measures (but not disease severity)

→ Psychological distress was related to cognitive performance but objective cognitive performance was not related to cognitive complaints



62

---

---

---

---

---

---

---

---

### Long COVID-19 Cognitive Outcomes – Children

Long-COVID clinical sample versus healthy controls Morrow et al., (2021)	Decreased quality of life scores  Subset of patients with difficulties with sustained auditory attention and divided attention – but most had preexisting attention/mood concerns  Self-reported elevated depression and anxiety
---	--



63

---

---

---

---

---

---

---

---

### COVID-19/Long COVID Deficits(?)

\*research is mixed!

Attention and Executive Functions
Learning and Memory
Processing Speed
Psychiatric Symptoms
Quality of Life



64

---

---

---

---

---

---

---

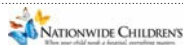
---

### Long COVID in Kids – Management

Multiple symptoms impacting lots of body systems

Many providers can be involved (in isolation or together)

- Specific Long COVID multidisciplinary clinics
- Existing specialty clinics that will see children with Long COVID
- Individual providers who see children with Long COVID
- Other??



65

---

---

---

---

---

---

---

---

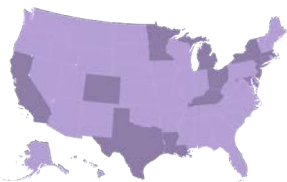
### 14 Pediatric Long COVID Clinics in US

Multidisciplinary clinics made up of multiple providers in a single location

Specifically aimed at addressing Long COVID

Some have waitlists several months long

Some have found that parents will visit multiple clinics



- Connecticut
- California
- Colorado
- Kentucky
- Louisiana
- Maryland
- Massachusetts
- Michigan
- Minnesota
- New Jersey
- New York
- Ohio
- Texas
- Washington, DC



66

---

---

---

---

---

---

---

---

### Long COVID in Kids – Individual Providers

Infectious Disease

Physical Medicine and Rehabilitation

Pulmonology

Cardiology

Neurology

NATIONWIDE CHILDRENS  
The world and a better way to live.

67

---

---

---

---

---

---

---

---

### Long COVID Management Key Components

<p><b>VALIDATION, VALIDATION, VALIDATION</b></p> <ul style="list-style-type: none"> <li>• Acknowledge reality of symptoms</li> <li>• Acknowledge the range of possible causes</li> </ul>	<p><b>Well-rounded approach to manage multiple symptoms</b></p> <ul style="list-style-type: none"> <li>• Symptom management (pain, fatigue, etc.)</li> <li>• Activity recommendations (pacing, breaks, build endurance, etc.)</li> <li>• Coping and adjustment</li> </ul>
--	---

NATIONWIDE CHILDRENS  
The world and a better way to live.

68

---

---

---

---

---

---

---

---

### COVID-19 and Educational Disruption

THE CLINICAL NEUROPSYCHOLOGIST  
<https://doi.org/10.1080/13854804.2023.1970239>

**Routledge**  
Taylor & Francis Group

[Check for updates](#)

The impact of COVID-19 related educational disruption on children and adolescents: An interim data summary and commentary on ten considerations for neuropsychological practice

Mary K. (Molly) Colvin\* , Jennifer Reesman\* and Tannahill Glen\*

\*Massachusetts General Hospital Harvard Medical School, Boston, MA, USA; \*Kennedy Krieger Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA; \*Neuropsychology, Inc., Jacksonville, FL, USA

NATIONWIDE CHILDRENS  
The world and a better way to live.

69

---

---

---

---

---


---

---

---

**COVID-19 and School: Most at Risk Groups**

Marginalized Groups	Early Learners	Children with Disabilities
---------------------	----------------	----------------------------

 The world's first and largest learning center

70

---

---

---

---

---


---

---

---

**10 New Considerations in Cognitive Assessment and Intervention**

- Reduced instruction and exposure to academic material
- Absenteeism, delays in starting school, etc.
- Educational technology issues (lack of access, inconsistent access, etc.)
- Variable plans to address learning loss (special education, grade retention, etc.)
- Special education disruptions (disrupted assessment, implementation, and access)
- Delays in evaluation, diagnosis, and treatment of learning issues
- Mental and physical health impact on cognitive performance
- Impact of COVID-related stressors on Adverse Childhood Experiences (ACE)
- Validity of remote evaluations and those using PPE/safety precautions
- Prolonged educational disruption and the impact on developmental trajectories

 The world's first and largest learning center Colvin, Reesman, & Glen 2021

71

---

---

---

---

---

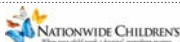
---

---

---

**Practice Implications for Cognitive Assessment and Intervention**

- Factors related to a child's instruction (curriculum, access, type of instruction, etc.) may impact their development/cognitive test performance
- Existing norms may or may not currently (or in the future) apply to certain children or certain groups of children
- Attendance and absenteeism (or delay of school for young children) may impact academic skill development
- Students most at risk, and with the least access to resources, are often most likely to be enrolled in distance learning
- Current diagnostic criteria may not apply (consistent exposure to instruction, symptoms in more than one environment, etc.)
- Mental/physical challenges, financial stress, etc. have increased during COVID-19 and may impact testing performance and development overall

 The world's first and largest learning center Colvin, Reesman, & Glen 2021

72

---

---

---

---

---

---

---

---



## AAPM&R Recommendations

TABLE 1: PASC cognitive symptom assessment recommendations



Recommendation	Notes
1. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.
2. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection who have had cognitive symptoms.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.
3. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection who have had cognitive symptoms and who are at high risk for cognitive impairment.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.
4. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection who have had cognitive symptoms and who are at high risk for cognitive impairment and who are also at high risk for mental health issues.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.
5. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection who have had cognitive symptoms and who are at high risk for cognitive impairment and who are also at high risk for mental health issues and who are also at high risk for academic impairment.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.
6. Screen for cognitive symptoms in all children and adolescents with COVID-19 infection who have had cognitive symptoms and who are at high risk for cognitive impairment and who are also at high risk for mental health issues and who are also at high risk for academic impairment and who are also at high risk for social impairment.	Screening should be performed by a clinician familiar with the child's baseline cognitive and behavioral functioning.

[https://www.aapm.org/docs/default-source/news-and-publications/covid/cognitive-symptoms-evidence-tables-030222.pdf?sfvrsn=3e3e287c\\_0](https://www.aapm.org/docs/default-source/news-and-publications/covid/cognitive-symptoms-evidence-tables-030222.pdf?sfvrsn=3e3e287c_0)

- Recommendations developed by multidisciplinary team
- Cognitive screening
  - Common symptoms and referrals
  - Neurocognitive assessment tools and interventions
  - Treatment recommendations
  - Health equity considerations



73

---

---

---

---

---

---

---

---

---

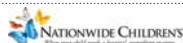
---

## COVID-19 Learning disorders

### COMMENT

Reforming learning disorder diagnosis following COVID-19 educational disruption

Mary K. Colvig<sup>1,2,3</sup>, Jennifer Reesman<sup>4\*</sup> and Tammy Hill Glen<sup>5</sup>



74

---

---

---

---

---

---

---

---

---

---

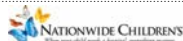
## COVID-19 and Learning Disorders

### LD Diagnostic Criteria (DSM-V summary)

- Academic skills are below age expectations on comprehensive assessment
- Academic impairments interfere with everyday functioning
- Learning problems >6 months even with intervention
- Not related to psychosocial factors or lack of exposure

### Diagnostic Errors

- If an LD is missed because it is attributed to lack of exposure/psychosocial factors → delayed services
- If an LD is incorrectly diagnosed → misdiagnosis and unnecessary intervention



75

---

---

---

---

---

---

---

---

---

---

### Solutions from Colvin et al.

Improve recognition of clinical symptoms and risk factors

- LDs are brain based disorders that occur during development
- Understand other factors which may signal an LD (speech delays in reading LD)

Consider a provisional diagnosis

- Can initiate interventions sooner
- Document COVID-19 school interruption
- Consider pre-pandemic academic functioning
- Eliminate >6 month intervention criteria

Prioritize the most vulnerable students for assessment and intervention

- Advocate for children who are the greatest risk
- Consider IDEA criteria which slightly differ from DSM-V (no formal diagnosis needed for services)



Colvin, Reesman, & Glen 2022

76

---

---

---

---

---

---

---

---

### New things to consider

Type of academic instruction, quality, duration, etc.

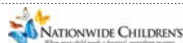
Chronic absenteeism during pandemic?

Overall development and pre-pandemic school performance

Reports from multiple informants of child's development and functioning

Pandemic specific questions

- New stressors?
- Coping and adjustment?



Colvin, Reesman, & Glen 2021

77

---

---

---

---

---

---

---

---

### COVID-19 and School: Most at Risk Groups

Marginalized Groups

Early Learners

Children with Disabilities



78

---

---

---

---

---

---


---

---


## Proposed battery / Domains to consider

ANALYSIS & PERSPECTIVE

**Postacute/Long COVID in Pediatrics**  
*Development of a Multidisciplinary Rehabilitation Clinic and Preliminary Case Series*  
Amanda K. Morrow, MD, Rowena Ng, PhD, Gray Burgess, PhD, Daniel Tenenbaum, PhD, Ellen Henning, PhD, Nika Sitton, PT, DPT, and Laura A. Malone, MD, PhD



See table on next slide.

 **NATIONWIDE CHILDREN'S**  
The world's best and a better way to live.

79

---

---

---

---

---

---

---

---

**TABLE 1.** Outpatient neuropsychological screening protocol applied through traditional in-person and novel telehealth assessment models

	3-4 yrs	5-7 yrs	8-11 yrs	16-17 yrs	18+ yrs
<b>Cognitive Constructs</b>					
Verbal skills	DAS-II Naming Vocabulary (5-6 yrs) or WASH-II Vocabulary (6-10 yrs)	DAS-II Naming Vocabulary (5-6 yrs) or WASH-II Vocabulary (6-10 yrs)	WASH-II Vocabulary	WASH-II Vocabulary	WASH-II Vocabulary
Nonverbal reasoning	DAS-II Matrices	DAS-II Matrices (5-6 yrs) or WASH-II Matrices Reasoning (6-10 yrs)	WASH-II Matrices Reasoning	WASH-II Matrices Reasoning	WASH-II Matrices Reasoning
Working memory	DAS-II Digit Forward	DAS-II Digit Forward	WISC-IV Digit Span; TFLC's Span and Span-IT	WASH-II Digit Span; CPM Sequences	WASH-II Digit Span; TEA-2 Elevator Counting and Elevator Counting; WISC-III Digit Span
Processing speed	---	NPPVT-II Inhibition, Naming, and Switching	Oral SBMT	Oral SBMT	Oral SBMT
Executive function	---	NPPVT-II Inhibition and Switching	DKFPS Verbal Fluency	DKFPS Verbal Fluency	DKFPS Verbal Fluency
Verbal memory	---	CHAMP List	CHAMP List	CHAMP List	CVLS-3
Performance validity indicator	---	MOY Natural	MOY Natural	MOY Natural	MOY Natural
<b>Questionnaires (Caregiver Report)</b>					
Psychosocial and behavior	Conners Early Childhood (3-5 yrs)	Conners Early Childhood (5-7 yrs)	CBRS	CBRS	BASC-3, CBARS
Executive functioning	BEIIF-P	BEIIF-P	BEIIF-2	BEIIF-2	BEIIF-2, BEIIF-A
Behavioral concerns	ADHD-RS-5 (5+ yrs), YBRS ODD/CD (6+ yrs), RCAD, Anxiety, Depression, B-CAD, Anxiety, Depression, DCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), YBRS ODD/CD (6+ yrs), RCAD, Anxiety, Depression, B-CAD, Anxiety, Depression, DCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), YBRS ODD/CD (6+ yrs), RCAD, Anxiety, Depression, B-CAD, Anxiety, Depression, DCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), YBRS ODD/CD (6+ yrs), RCAD, Anxiety, Depression, B-CAD, Anxiety, Depression, DCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), YBRS ODD/CD (6+ yrs), RCAD, Anxiety, Depression, B-CAD, Anxiety, Depression, DCD subscales (6+ yrs)
<b>Questionnaires (Self-report)</b>					
Anxiety	RCMAS-2 (6-7 yrs), MASC-2 (8-10 yrs)	RCMAS-2 (6-7 yrs), MASC-2 (8-10 yrs)	RCMAS-2 (6-7 yrs), MASC-2 (8-10 yrs)	RCMAS-2 (6-7 yrs), MASC-2 (8-10 yrs)	BAI
Depression	CDR-2 (7-17 yrs), BDI-2 (11+ yrs)	CDR-2 (7-17 yrs), BDI-2 (11+ yrs)	CDR-2 (7-17 yrs), BDI-2 (11+ yrs)	CDR-2 (7-17 yrs), BDI-2 (11+ yrs)	BDI-2

80

---

---

---

---

---

---

---

---

## General Recommendations

### Return to school

- Encourage regular attendance
- Consider gradual return (if prolonged absence)
- Consider modified schedule
- Understand there may be “good days and bad days”
- Have a place for breaks when symptoms flare
- Focus on attendance NOT academic success

 **NATIONWIDE CHILDREN'S**  
The world's best and a better way to live.

81

---

---

---

---

---

---

---

---

### General Recommendations

#### Physical symptoms

- Focus on successes (even small) to build confidence
- Do not conduct repeated symptom assessments
- Express understanding, support, and a shared belief that the child will get better
- Physical therapy
- Sometimes medication
- Eat healthy and stay hydrated
- Rescue plan for symptom flares




---

---

---

---

---

---

---

---

82

### General Recommendations

#### Pacing

- Stand up, stretch, move around during the day
- Schedule breaks during the day
  - Modify schedule during the day
  - Stick to breaks to avoid “overdoing” it
- Modify assignments
  - Reduce workload volume
  - Provide oral reports versus written
  - Give copies of notes or use a scribe
  - Extended time
  - Help create a schedule if staying on top of work is hard




---

---

---

---

---

---

---

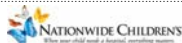
---

83

### General Recommendations

#### Sleep (which can be disrupted after COVID-19)

- Stop using electronics 30-60 minutes before bed
- Shoot for 8 hours of sleep each night
- Keep a regular schedule
- Avoid naps (if possible)
- Don't stay in bed more than 10 minutes without falling asleep
- Only sleep in bed
- Avoid caffeine after noon
- Exercise regularly
- Have a quiet, dark, cool sleep space
- Try a relaxing bedtime routine




---

---

---

---

---

---

---

---

84

## General Recommendations

### Emotional health

- Focus on functioning
- Gradual return to activities
- Behavior activation
- Maintain a routine and schedule
- Acknowledge and address worries/thoughts
  - e.g., Instead of "I'm never going to feel better", "This won't last forever, I am going to have a good day no matter what".
- Mindfulness-based strategies
- Recognize that pre-existing anxiety and/or mood concerns may be exacerbated by COVID and more formal interventions may be necessary (therapy, medication)



85

---

---

---

---

---

---

---

---

---

---

## Thank you!



### Questions?

Contact [Christine.Koterba@nationwidechildrens.org](mailto:Christine.Koterba@nationwidechildrens.org)  
[Kristen.Hoskinson@nationwidechildrens.org](mailto:Kristen.Hoskinson@nationwidechildrens.org)



86

---

---

---

---

---

---

---

---

---

---

## References

- Ahmed, M., Advani, S., Moreira, A., Zorelic, S., Martinez, J., Chorath, K., Acosta, S., Naqvi, R., Burmeister-Morton, F., Burmeister, F., Tarruela, A., Petershack, M., Evans, M., Hoang, A., Rajasekaran, K., Ahuja, S., & Moreira, A. (2020). Multisystem inflammatory syndrome in children: A systematic review. *EClinicalMedicine*, 26, 100527. <https://doi.org/10.1016/j.eclim.2020.100527>
- Albano, A.M., McGuire, J.L., Kanthimathinathan, H.K., Rao, J.D., & Fink, E.L. (2021). Worldwide epidemiology of neuro-coronavirus disease in children: Lessons for the next pandemic. *Current Opinion in Pediatrics*, 33, 580-90. doi: 10.1097/MOP.0000000000001069
- Bhogal, A., Borg, B., Jovanovic, T., & Marusak, H.A. (2021). Are the kids really alright? Impact of COVID-19 on mental health in a majority Black American sample of school children. *Psychiatry Res*, 304, 114146. doi: 10.1016/j.psychres.2021.114146.
- Buonsenso, D., Mumbili, D., De Rose, C., Sinatti, D., Ricchiuto, A., Carfi, A., & Vezzolini, P. (2021). *Acta Paediatrica*, 110(7), 2208-2211. doi: 10.1111/apa.15870
- Centers for Disease Control and Prevention (2021, December 14). *Health department-reported cases of multisystem inflammatory syndrome in children (MIS-C) in the United States*. <https://www.cdc.gov/covid-data-tracker/mis-national-surveillance>.
- Colvin, M., Reesman, J., & Glen, T. (2021). The impact of COVID-19 related educational disruption on children and adolescents: An interim data summary and commentary on ten considerations for neuropsychological practice. *The Clinical Neuropsychologist*, 8, 1-27. DOI: [10.1080/13804495.2021.1979330](https://doi.org/10.1080/13804495.2021.1979330).
- Colvin MK, Reesman J, Glen T. Reforming learning disorder diagnosis following COVID-19 educational disruption. *Nat Rev Psychol*. 2022;1(5):251-252. doi: 10.1038/s41598-022-00052-0. Epub 2022 Apr 7. PMID: 35541282; PMCID: PMC908098.
- Feldstein, L.R., Rose, E.B., Horwitz, S.M., Collins, J.P., Newhams, M.M., Son, M., Newburger, J.W., Kleinman, L.C., Heidemann, S.M., Martin, A.A., Singh, A.R., Li, S., Tarquinio, K.M., Jaggi, P., Oster, M.E., Zackai, S.P., Gillen, J., Ratner, A.J., Walsh, R.F., Fitzgerald, J.C., ... CDC COVID-19 Response Team (2020). Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *The New England journal of medicine*, 383(4), 334-346. <https://doi.org/10.1056/NEJMoa2021680>
- Fenlon, E.P., Chen, S., Ruzal-Shapiro, C.B., Jaramillo, D., Maddocks, A.B.R. (2021). Extracardiac imaging findings in COVID-19-associated multisystem inflammatory syndrome in children. *Pediatric Radiology*, 51, 831-9. doi: 10.1007/s00247-020-04929-1



87

---

---

---

---

---

---

---

---

---

---

### References

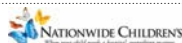
- Kaushik, S., Aydin, S. I., Derespina, K. R., Bansal, P. B., Kowalsky, S., Trachman, R., Gillen, J. K., Perez, M. M., Sosnick, S. H., Conway, E. E., Jr, Berzow, A., Seiden, H. S., Passi, R. H., Uthay, H. M., Ofon-Amanhin, G., & Medar, S. S. (2020). Multisystem Inflammatory Syndrome in Children Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (MIS-C): A Multi-institutional Study from New York City. *The Journal of pediatrics*, 224, 24–29. <https://doi.org/10.1016/j.jpeds.2020.08.045>
- Lin, J. E., Ashour, A., Sewell, T. B., Hooe, B., Pryce, P., Earley, C., Shen, M. Y., Kemer-Rossi, M., Thakur, K. T., Vargas, W. S., Silver, W. G., & Genestlav, A. S. (2021). Neurological issues in children with COVID-19. *Neuroscience letters*, 743, 135567. <https://doi.org/10.1016/j.neulet.2020.135567>
- Lurie Children's Blog. (2021, May 27). *Children's mental health during the COVID-19 pandemic*. Lurie Children's Blog. <https://www.luriechildrens.org/en/blog/childrens-mental-health-pandemic-statistics/>
- Maitzou, H. C., Pavli, A., & Tsakris, A. (2021). Post-COVID Syndrome: An insight on its Pathogenesis. *Vaccines*, 9(5), 497. <https://doi.org/10.3390/vaccines9050497>
- Matteudi, T., Luciani, L., Fabre, A., Minodier, P., Boucekin, M., Bosdure, E., Dubus, J.C., Colson, P., Chabrol, B., Morand, A. (2021). Clinical characteristics of paediatric COVID-19 patients followed for up to 13 months. *Acta Paediatr*, 110(12), 3331-3333. doi: 10.1111/apa.16071.
- Narvegeni, S. I., Koloivos, G., Tsimpis, V., Kafetzis, D., Tsotas, G., & Fotis, L. (2021). The importance of heart and brain imaging in children and adolescents with Multisystem Inflammatory Syndrome in Children (MIS-C). *Rheumatology International*, 41, 1037-44. doi: 10.1007/s00286-021-04845-z
- Nagata, J. M., Cortez, C. A., Cattle, C. J., Ganson, K. T., Iyer, P., Bibbins-Domingo, K., & Baker, F. C. (2022). Screen time use among US adolescents during the COVID-19 pandemic: Findings from the adolescent brain cognitive development (ABCD) study. *JAMA pediatrics*, 176(1), 94-96.



88

### References

- Nepal, G., Shrestha, G. S., Rehg, J. H., Gajurel, B. P., Ojha, R., Agrawal, A., Panthi, S., Khatri, B., & Adhikari, I. (2021). Neurological Manifestations of COVID-19 Associated Multi-system Inflammatory Syndrome in Children: A Systematic Review and Meta-analysis. *Journal of Nepal Health Research Council*, 19(1), 10–18. <https://doi.org/10.33314/jnhrc.v19i1.3410>
- Palabiyik, F., Ackay, N., Sevketoglu, E., Hatipolu, N., Sari, E.E., & Inci, E. (2021). Imaging of multisystem inflammatory disease in children with MIS-C associated with COVID-19. *Academic Radiology*, 28, 1200-8. doi: 10.1016/j.acra.2021.05.030
- Pennes, J., Abdel-Mannan, O., Grant, K., et al. (2021). 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: A retrospective cohort study. *Lancet. Child and Adolescent Health*, 5, 473-82. doi: 10.1016/S2352-4642(21)00138-3
- Principi, N., & Esposito, S. (2021). Are we sure that the neurological impact of COVID 19 in childhood has not been underestimated?. *Italian journal of pediatrics*, 47(1), 191. <https://doi.org/10.1186/s13052-021-01144-y>
- Saatci, D., Ranger, T.A., Garriga, C., et al. Association Between Race and COVID-19 Outcomes Among 2.6 Million Children in England. *JAMA Pediatr*. 2021;175(9):928-938. doi:10.1001/jamapediatrics.2021.1685Sandoval, F., Julio, K., Méndez, G., Valderas, C., Echeverría, A. C., Perinelli, M. J., Suarez, N. M., Barraza, G., Piñera, C., Alarcón, M., Samaniego, F., Quesada-Rios, P., Robles, C., & Izquierdo, G. (2021). Neurologic Features Associated With SARS-CoV-2 Infection in Children: A Case Series Report. *Journal of child neurology*, 36(10), 853-868. <https://doi.org/10.1177/0883207321989164>
- Schupper, A. J., Yaeger, K. A., & Morgenstern, P. F. (2020). Neurological manifestations of pediatric multi-system inflammatory syndrome potentially associated with COVID-19. *Child's nervous system : CNS : official journal of the International Society for Pediatric Neurosurgery*, 26(8), 1579-1580. <https://doi.org/10.1007/s00381-020-04755-8>
- Singer, T.G., Evankovich, K.D., Fisher, K., Demmler-Harrison, G.J., & Risen, S.R. (2021). Coronavirus infection in the nervous system in children: A scoping review making the case for long-term neurodevelopmental surveillance. *Pediatric Neurology*, 117, 47-63. doi: 10.1016/j.pediatrneurol.2021.01.007



89

### References

- Siracusa, L., Cascio, A., Giordano, S., Medaglia, A. A., Restivo, G. A., Pirone, I., Saia, G. F., Collura, F., & Colomba, C. (2021). Neurological complications in pediatric patients with SARS-CoV-2 infection: a systematic review of the literature. *Italian journal of pediatrics*, 47(1), 123. <https://doi.org/10.1186/s13052-021-01066-9>
- Ucan, B., Sahap, S.K., Cinar, H.G., Yildiz, Y.T., Uner, C., Polat, M., & Derinkuyu, B.E. (2021). Multisystem inflammatory syndrome in children associated with SARS-CoV-2: Extracardiac radiological findings. *British Journal of Radiology*, 95, 1-8. doi: 10.1259/bjr.20210570
- Zimmermann, P., Pibet, L., Curtis, N. (2021). How common is long COVID in children and adolescents? *The Pediatric Infectious Disease Journal*, 40 (12), 482-487. doi: 10.1097/PINF.0000000000000328
- Zimmermann, P., Pibet, L. F., & Curtis, N. (2022). The challenge of studying long COVID: an updated review. *The Pediatric infectious disease journal*, 41(5), 424-426.



90