Responses to Participants' Questions

This document provides responses to questions raised by webinar participants related to the following presentations:

- **Presentation 1:** ***Pediatric COVID-19 and MIS-C in the National COVID Cohort Collaborative (N3C)***
  Tellen D. Bennett, MD, MS

- **Presentation 2:** ***Leveraging the PEDSnet EHR Network Infrastructure to Inform Our Understanding of PASC and MIS-C***
  Ravi Jhaveri, MD, FPIDS, FAAP

- **Presentation 3:** ***GCS-NeuroCOVID Consortium: Pediatrics***
  Ericka L. Fink, MD, MS

Presentation 1: Questions and Responses

Q1. *In your study, was there any information on recovery of the lung conditions and fatigue?*

Response: We have information about hospital disposition, which is a coarse measure. Consequently, we're limited in our ability to capture long-term outcomes. Studies such as Dr. Fink's and others will be able to assess recovery after children and adults who developed lung conditions return home following hospitalization.

Q2. *I've been following the recent outbreak of hepatitis in children, in some cases requiring liver transplants. I'm wondering if SARS-CoV-2, while maybe not the inciting factor, could be involved. Perhaps SARS-CoV-2 is a cofactor or inducer causing a known agent, such as adenovirus 14, to produce a more virulent disease.*

Response: No one is sure, so I can't give a definitive answer. However, with some of our behavior changes resulting from the pandemic, we've seen differences in the ways viruses circulate in the population, particularly among children. We've seen other non-COVID respiratory diseases circulating at high levels outside of their normal season simply because of the changes in when and how children get together, go to school, etc. It's likely that the changes we're seeing are because of these behaviors. The pandemic also impacted who is exposed to viruses on a day-to-day basis and who is susceptible. Many of us have coincident infections that boost our local immunity

against future or more severe infections. It may be that these manifestations reflect a lack of infection with other organisms that might protect children against severe infection.

Presentation 2: Questions and Responses

Q3. *Since the CDC definition is predicated on inpatient admission, how can your team call outpatient cases MIS-C?*

Response: I agree that this is a challenge. Consequently, we want to dive deep to understand if these outpatients meet other criteria for MIS-C or if they have some other condition that is a "copycat" of MIS-C. If there are outpatients who do seem to have a milder version of MIS-C, then we need to consider modifying the case definition to include these patients.

Presentation 3: Questions and Responses

Q4. *In your study, were there specific preexisting conditions among the children at an increased risk of neurological manifestations of MIS-C?*

Response: We reported that 61% of children with acute COVID had preexisting conditions as compared with 37% of the children with MIS-C. The most common preexisting conditions among children with MIS-C were respiratory and neurological, at 13% and 9%, respectively. Only children with respiratory preexisting conditions were associated with having neurologic manifestation of any kind among MIS-C patients. Gastrointestinal preexisting diseases were associated with protection from neurological manifestations. I think a lot of these results point to generating hypotheses.

All Presenters: Questions and Responses

Q5. *Can you speak to the neurocognitive effects of Long COVID?*

Responses:

Dr. Fink: I'm not aware of any studies that have reported detailed neurocognitive outcomes. It will be very important to see the results from these types of studies. However, it will be challenging to tease out the general effects of the pandemic, such as missing school and friends. If studies are looking at outcomes such as school outcomes, emotional health outcomes, pain, and the ability to pay attention, it will be difficult to tease out the general effects of the pandemic unless we have a good control group. Nonetheless, we'll learn a lot about what children are going through during this pandemic. In our study, we don't assess these types of detailed

neurocognitive outcomes. However, we will look at some gross multidimensional categories of function, health impact on the quality of life, and how the family is functioning.

Dr. Bennett: I completely agree that those are among the most meaningful outcomes. I think that they'll be best elucidated in linkage between prospectively collected gold standard outcomes and the rich electronic health record data about the encounter experience when patients were more ill. Teaming up these two data sources will provide the best information and RECOVER has plans along these lines.

Webinar Slides

To request a copy of the R3 Webinar slides, please email RECOVER_ACC@rti.org.

To Learn More

- Information about RECOVER research and to volunteer for studies: https://recovercovid.org/research
- Frequently Asked Questions about RECOVER and PASC: https://recovercovid.org/faqs
- CDC information: Information for the general public and for healthcare providers about post-Covid conditions: https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/

References

Fink EL, Robertson CL, Wainwright MS, et al. Prevalence and risk factors of neurologic manifestations in hospitalized children diagnosed with acute SARS-CoV-2 or MIS-C. *Pediatr Neurol.* 2022;128:33-44. https://doi.org/10.1016/j.pediatrneurol.2021.12.010

Forrest CB, Burrows EK, Mejias A, et al. Severity of acute COVID-19 in children <18 years old March 2020 to December 2021. *Pediatrics. 2022;149(4)*:e2021055765. https://doi.org/10.1542/peds.2021-055765

Martin B, DeWitt PE, Russell S, et al. Characteristics, outcomes, and severity risk factors associated with SARS-CoV-2 infection among children in the US National COVID Cohort Collaborative. *JAMA Netw Open. 2022;*5(2):e2143151. doi: 10.1001/jamanetworkopen.2021.43151