Responses to Participants' Questions

The overarching goal of the RECOVER Research Review (R3) Seminars is to catalyze a shared understanding of the research being conducted by the scientific stakeholder community within the RECOVER Consortium. The R3 Seminars and the Q&As typically feature highly scientific material intended for researchers and clinicians. For other audiences interested in these topics, a link to the National Library of Medicine's MedlinePlus medical dictionary is provided at the end of the Q&As as a resource to help in understanding the scientific terminology.

This document provides responses (edited for clarity) to questions raised by seminar participants related to the following presentations at the R3 Seminar *Social Determinants of Health and Long COVID: Insights from the RECOVER Observational Studies* held on October 14, 2025 (videos for this and previous seminars are available from the Seminar Series page on the RECOVER website):

- ***Social Determinants of Health and Long COVID: Insights from the RECOVER Observational Studies***
  Candace H. Feldman, MD, MPH, ScD
- ***Social Determinants of Health Risk and Resiliency Factors Associated with Long COVID in Pediatrics***
  Kay E. Rhee, MD, MSc, MA
- ***RECOVER Community Representative: Brittany D. Taylor, MPH***
- ***Discussant: Elizabeth W. Karlson, MD, MS***

All Presenters: Questions and Responses

Q: Have you found that there are disparities in Long COVID awareness among different demographic groups? How do you think those disparities might affect our statistics and our analyses? Could we address these gaps?

Response:

Ms. Taylor: There were some disparities in who participated in our studies, and that subsequently affected our findings and results. Our research found that we have higher educational attainment levels for RECOVER participants, as three-fourths of our participants have a college degree. That is not always the case when you're looking at research studies and when you're working with populations for studies. Diversifying may mean adjusting the ways that we are recruiting patients and which communities we are going into. I know that we made concerted

efforts, like working with the Boston COVID Recovery Cohort (BCRC). By integrating ourselves into more community-based settings, showing up in areas where we know more trusted messengers are located and communicating with those trusted messengers in religious settings, or checking out your local soccer league, things of that nature, where we can communicate with individuals who might not have a college-level education, we can reach a more varied population. When we're raising awareness in those areas and in those venues, then we'll be able to recruit a more diverse population. So, there are a couple of disparities, but changing the way we recruit and communicate about Long COVID would help to diversify participants and subsequent results.

Q: What's unique about assessing social determinants of health in children? It seemed that you had a lot of caregiver factors. Did you have questionnaires that were designed specifically to assess social determinants of health among the caregivers?

Response:

Dr. Rhee: In my opinion, it's always trickier in pediatrics to try to get at what the child is experiencing when you have someone as young as 6 or 7 years old. You do have to rely on somebody else to report what they think the child is experiencing. So, a lot of the social determinants of health factors that we assessed were family, household, environmental, and social environments around the child, as well as, as best as we could, what the child was experiencing. We didn't develop any questionnaires ourselves. We used pre-existing, validated ones. But we did get at things like, "Is the *child* experiencing discrimination?" or "Is the *parent* experiencing discrimination?" We were also looking at access to childcare and things like that. We also included a lot of measures around the parent's mental health status and social support, because the child's family environment is the most proximal to the child in determining a lot of outcomes—academic outcomes, social-emotional development, health outcomes. We included a lot of parent mental health measures, but we did not include them in this analysis. We are actually finding some interesting things there as well, which will hopefully be a different manuscript. But yes, it is a little bit trickier to tease this apart for the child.

Q: Can you describe for us what kinds of things you measured in the social environment domain? Were the questions about the household environment similar to the questions about household environment in the RECOVER pediatric cohort study?

Response:

Dr. Feldman: There were questions that related to concepts of household support and neighborhood support—less so about the inter- or intra-household dynamics. The social support questionnaire that we used was similar to what Dr. Rhee was describing for the pediatric cohort analysis. All questionnaires that we used were validated; they had been studied in other populations. The social support questionnaire included questions like, "Do you

have someone who can take you to the doctor? Someone who can help you if you can't get out of bed?" It also asks if you have somebody who understands your problems, someone to love or make you feel wanted. The other sort of questions that we asked in that domain, as you mentioned, were the marital status question, as well as a broader neighborhood support question: Do you live in a neighborhood where people help each other out? Are there people in your neighborhood whom you feel you can count on?

Q: RECOVER has collected a lot of blood samples from the pediatric and the adult cohort participants. Do you anticipate that you could try to understand the biologic underpinnings of these findings by using these samples?

Response:

Dr. Rhee: That's the hope. I really would love to do that. I think also in the chat, somebody asked about the acute phase of the infection, the viral titers, and the immune response. Unfortunately, at least in pediatrics, we were not always enrolling participants at the time of their infection. We were often enrolling them after the infection and having them report on some of their symptoms. That was when the blood was collected. So, unfortunately, as Dr. Feldman had mentioned before, you really need a prospective study where you're able to collect blood at the moment of infection to look at those titers. But that said, I do think there's a lot of potential with the biosamples. We have to look at some of the immune markers like cytokines. I'm not involved in those working groups right now, so I don't know what tests they're planning to do, but it would be really important to understand the mechanisms of why some people are at risk, and for families, adults, and children who have experienced more stressors, whether there is something different about their biology that makes them more susceptible to getting the infection, then potentially not clearing the infection, thus having the post-viral syndrome that persists that we call Long COVID. For this reason, the advocacy that's needed to help people understand that these social factors have a real impact on physiologic, biologic, and mental health outcomes is important. These factors are linked, and if we can help people understand that, I'm hoping we can make some changes on multiple fronts: the biologic front and the social-political front.

Q: Could analysis of biomarkers during the acute infection period lead to understanding the biology of Long COVID and treatment?

Response:

Dr. Feldman: I'm a rheumatologist, so the biomarkers that we think about are acute-phase reactants, like cytokines that show inflammation. There have been a number of studies among people who've experienced stress or extreme stress that show significantly higher biomarkers or markers of inflammation in the body. The challenge is teasing apart the cause. We certainly know that people who live with chronic stress oftentimes have, at baseline,

higher markers of inflammation, or at least that's been shown in a number of studies. Having an infection also causes inflammation. I think one thing, and Dr. Rhee alluded to this as well, that would be very interesting is whether there is a difference in the pattern of these biomarkers over time in people who are exposed to acute infection and then live in social situations that contribute to chronic stress. I would hypothesize that we would find a potential difference, and that would be one mechanism to think about. The other two things that came to my mind are understanding the microbiome and the way that could play a role. We know that poverty, food insecurity, and housing instability contribute to the microbiome and the dynamics between different cytokines and biomarkers as well. And so, thinking longitudinally as well could be very interesting. The last point I'd make, too, is something that's been studied a lot, less in this specific field and less by rheumatologists, are the biological mechanisms by which adverse environmental exposures like air pollution may impact susceptibility to chronic conditions and autoimmune conditions. The ability to think about the role an environmental exposure might play based on where a person lives in terms of their risk might help us understand a piece of this as well.

Q: Are there disparities in Long COVID awareness among different demographic groups? Could this further affect our statistics, and how can we address these gaps?

Responses:

Dr. Feldman: Sure. Ms. Taylor did comment on this, and I agree with her response. While we didn't directly ask participants if they had been diagnosed with Long COVID, we did ask about a number of different symptoms, and people may perceive and describe symptoms differently depending on their experiences with healthcare in the past, their cultural backgrounds, their language, and their lived experiences. It is possible that how we asked about the symptoms may not have captured everybody's experiences the same way. It is therefore possible that the Long COVID Research Index may not represent everybody equally.

Dr. Rhee: I just wanted to add to that. I think this issue of making sure that we got a broad demographic in both our cohorts was something very important because it would allow us to get different perspectives and different experiences. We also used the Long COVID Research Index, so we asked about symptoms. We didn't ask someone if they had Long COVID. So, regardless of whether or not somebody thought they had Long COVID, we were collecting a compilation of symptoms for which we then created a research index. This approach has pros and cons. It helps to more objectively look at clusters of symptoms that are prevalent, but it doesn't capture everything, and there may be people who didn't fit the research index because they didn't have enough symptoms, or they had only one very severe symptom. Were there people who didn't realize they had Long COVID, or were we not reaching populations that may have experienced Long COVID differently? Possibly. But I think we tried to get around those issues as much as we could by recruiting from diverse areas of our country. One thing we haven't mentioned much is the rural population and the medically underserved population. In the pediatric cohort,

about 30%–40% of the population was medically underserved, not rural. Rural populations were more difficult to recruit, which is the case in all national studies. But by getting the medically underserved population, we are hoping to also recruit people who may not have been accessing healthcare regularly and still capture their symptoms.

Q: Are there any insights gleaned from the pregnancy subgroup?

Response:

Dr. Feldman: There were 209 pregnant women in the cohort with acute COVID who are followed prospectively. There's a separate body of literature and a set of studies happening in that pregnancy cohort that will glean insights in a much deeper way than what I can provide. We tried to address several questions in our manuscript. The first was, "Is there any chance that we are misclassifying Long COVID in pregnant women?" because several of the symptoms in the definition of Long COVID could be symptoms of pregnancy, such as post-exertional malaise or fatigue. We did compare pregnant women versus nonpregnant women and men as well and looked at each of the components of the Long COVID Research Index. What we found, overall, was that the percentage of pregnant women with Long COVID in this acute cohort was about 7.7%, whereas in nonpregnant women, it was closer to 12%. There was a lower percentage of pregnant women who met the definition of Long COVID compared with nonpregnant women. Similarly, there was a lower percentage of pregnant women who had each of the components of the Long COVID Research Index, so there were fewer with palpitations, thirst, brain fog, and so on. Another question we were asked was, "If we removed pregnant women from the cohort, was there a stronger or weaker association between social determinants of health and Long COVID?" When we did this, we really found no difference. So, it seems like the association between social risk factors and Long COVID is very similar for pregnant women compared with nonpregnant women. Due to the small numbers of pregnant women with Long COVID in this specific subcohort (n=16), we couldn't look at direct associations between social risk factors and development of Long COVID. When we excluded these individuals, there was no significant difference from the overall population. I would direct you to the pregnancy studies, including published studies from RECOVER, for a much more in-depth understanding. They are also looking at social risk factors in that specific cohort.

Q: What were the reasons behind the difference in the sample size between the school-age and adolescent groups?

Response:

Dr. Rhee: In the adolescent cohort, we were able to recruit from the Adolescent Brain Cognitive Development (ABCD) Study, which has been going on since 2016. Prior to COVID, they had recruited 11,000 children or adolescents into their study and were following them. We partnered with ABCD, so we were able to recruit a lot of adolescents very quickly because they were in an already-existing cohort. Overall, with the 30-plus RECOVER sites, we were recruiting children and adolescents. It was just more difficult to enroll children because we weren't recruiting from an already existing research cohort. That's why you see a discrepancy in the numbers between grade-school children and adolescents.

Q: We know that reinfection is a risk factor for Long COVID and more severe Long COVID. What social determinants of health might be associated with reinfection?

Responses:

Dr. Rhee: We haven't done that analysis yet. I think it's an interesting question. I'd have to go back and see how much information we've gathered about repeat infections because there's a cohort of people who moved into Tier 2, and we are gathering serial questionnaire data from them.

Dr. Feldman: Yes, I agree. We haven't looked at it yet, but I think it is a very interesting question. There is another interesting question, too, which is the ability to have recovery time after infection, the degree to which that timing may contribute to Long COVID, and how social risk factors play a role. This also relates to reinfection risk. Can you minimize your exposure after your first infection? My hypothesis is that individuals with a higher burden of social risk factors will have less rest time post-infection and a higher risk of subsequent infection. We haven't studied it, but both are very interesting and important questions.

Q: In the Risk Factors Table 2 in the slide deck, are these factors encompassing these social risk factors at any time? Or just before developing Long COVID?

Response:

Dr. Karlson: All of the social risk factors were assessed at the baseline survey, completed within 1 month of the infection. Long COVID was defined as 6 months or longer after baseline.

Q: Is there any information on whether people who develop PASC had the same or less opportunity to rest (take off work, relieved from home responsibilities like childcare) than people who did not?

Response:

Dr. Feldman: Interesting question! Our focus, though, was on the risk for developing Long COVID (not the time period after). We didn't have that information for the time following infection either, but I would hypothesize that individuals with social risk factors would have had less of an ability to rest or take time off from work compared with those without these risk factors.

Q: Did the study look at Long COVID rates in individuals who live in poverty and live alone/with no family or social supports as opposed to individuals who live in poverty and crowded households?

Response:

Dr. Feldman: Great question. We did not look at these specific combinations in the adult study, but I agree that it would be interesting to see if there is a difference.

Q: What languages were available for the survey? Was it just English and Spanish?

Response:

Dr. Feldman: English, Spanish, and Chinese were available.

Q: What about the patients who were infected before 2021?

Response:

Dr. Karlson: The RECOVER adult cohort also enrolled participants who had COVID-19 as far back as March 2020, in the "post-acute cohort." This cohort also answered survey questions when they enrolled, but because they could potentially have had Long COVID at that time point, they were not included in this analysis. The post-acute cohort has been included in multiple other analyses and papers from RECOVER.

Q: In reference to the question about whether rest time during acute infection plays a role in Long COVID prevalence, are any panelists aware of complete or ongoing research in this area? Patients need paid leave for COVID, and having these kinds of data is a critical part of advocating for policy change.

Response:

Dr. Rhee: I'm not sure of any studies examining this question.

Q: From my understanding, for every 1-point increase in an adverse childhood experience (ACE) score, the risk for developing an autoimmune disease increases by about 20%. A score of four or more ACEs is significantly associated with higher probabilities of having a variety of chronic health conditions. Have ACEs been explored as either a risk factor for Long COVID, an outcome of Long COVID, or both?

Response:

Dr. Rhee: Many of the social determinants of health factors we measured in RECOVER (like food insecurity, housing insecurity, parental separation, and parent mental health issues) are also considered ACEs. Adverse social determinants of health and ACEs cause stress in a child and can result in a chronic stress response. So, although we did not ask about abuse, neglect, or witnessing violence in the home, I would suspect that these factors may also contribute to an increased risk of Long COVID.

Q: Were these social risk factors also linked to disease severity during the acute phase of infection? What about viral titer during the acute phase?

Response:

Dr. Feldman: We did not examine these specific questions. We did adjust for hospitalization for acute infection as a marker of disease severity in our analyses and found that after accounting for this factor, the associations between social risk factor presence and risk of Long COVID persisted.

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- CDC information: Information for the general public and for healthcare providers about post-COVID conditions.
- For medical/scientific terminology: MedlinePlus's Health Topics.