

# Transcript

## Claire Quiner:

Welcome to the RECOVER Research Review or R3 Seminar. My name is Claire Quiner and I am an epidemiologist with the RECOVER Administrative Coordinating Center and the moderator of today's seminar. The goal of this seminar series is to catalyze a shared understanding of the research within the RECOVER Consortium. I'd like to start by thanking everyone who submitted questions in advance. Please submit any questions that arise during today's presentation using the Q&A feature in Zoom. After the presentation, we'll answer as many questions as possible. A Q&A document will be posted with the recording of the seminar on [recoverCOVID.org](https://recoverCOVID.org). It will include the answers for submitted questions relevant to today's presentation. Questions about other scientific topics will be addressed in future seminars and answers to broader questions about RECOVER will be available and the FAQs at [recoverCOVID.org](https://recoverCOVID.org). As a reminder, we cannot answer individual questions about clinical care.

Our presenters today are Dr. Igbo Ofotokun, Dr. Melissa Stockwell and Dr. James Stone, as well as Brittany Taylor. Dr. Ofotokun is an accomplished clinician scientist whose career is devoted to combating the long-term sequelae of HIV, particularly among underrepresented populations. His work is focused on the threat and age related comorbidities posed to healthy aging in persons with HIV and the disproportionate burden in women. He leads an innovative global research collaboration to understand the pathobiology of these phenomena and has demonstrated that age-related comorbidities may be driven by disruption in the organ immune interface and amendable target. The higher burden in women may relate to synergy between gonadal impairment and chronic inflammation. Drawing on his HIV experience, he now leads the Atlanta hub of the NIH RECOVER effort aimed at understanding the post-acute sequelae of COVID-19. Dr. Melissa Stockwell is the Chief of the Division of Child and Adolescent Health and the Felice K. Shea Professor of Pediatrics in the Department of Pediatrics at Columbia University's College of Physicians and Surgeons.

She's also the founding director of the Department of Pediatrics Center for Children's Digital Health Research and a pediatrician in a New York Presbyterian Hospital Associated Community Clinic. Dr. Stockwell's Research Program, which concentrates on underserved children and adolescents, focuses on interventions to improve vaccinations with an emphasis on health technology and health literacy, as well as on respiratory infections and long COVID. Dr. Stockwell serves as the contact PI for the Columbia University hub site for recover and is the convening chair of Recover Pediatric Coordinating Committee. Dr. James Stone is the director of the Autopsy Service and head of the Cardiovascular Pathology Service at the Massachusetts General Hospital and an associate professor of pathology at Harvard Medical School. He is a site principal investigator for the RECOVER Autopsy cohort and member of the RECOVER Steering Committee. He is the past president of the Society for Cardiovascular Pathology. He has published multiple publications regarding the pathology of COVID-19, including international and international multicenter study describing the spectrum of cardiac changes associated with SARS-CoV-2 infection.

Ms. Brittany Taylor is the Community Impact Director with the American Heart Association, where she drives equitable health and wellbeing in the areas of hypertension control, nutrition security, tobacco sensation and diabetes prevention towards removing barriers to healthcare access and improving quality health across Georgia communities. She possesses 14 years of experience overseeing and implementing projects focused on health equity advancement, product disease management and prevention, infectious disease control, tobacco cessation and paternal health. Most recently she was jointly appointed to the chair to serve as co-chair for the National Community Engagement Group on RECOVER. As an invited reviewer, Brittany has conducted federal grant review for the HHS Office of the Assistant Secretary for Health, CDC, Johnson & Johnson Innovation as well as the EPA. Next slide please. The topic of today's seminar is RECOVER Observational Studies Consortium Update: Where are we and where are we headed? Today's speakers will share our current understandings, the gaps in our knowledge and how RECOVER will contribute to filling these knowledge gaps. With that, I'd like to hand it over to Dr. Ofotokun.

## Dr. Ofotokun

Thank you so much, Claire, for that introduction, and thanks everybody for joining this seminar. So I know that this is a very informed audience. Many of you follow the long COVID or post accurate sequela of COVID-19

science. So my goal today is to just provide a high overview of where we are in the field, some of the gaps and how RECOVER can fill in into those gap, and then provide a little bit of progress that we have made with the adult cohort of RECOVER and then talk about some of the things that are in the pipeline. So where are we? So we've learned a lot over the past two or three years. We now know the common symptoms that are associated with this new phenomenon known as long COVID. I think there's a general agreement that it's associated with fatigue, headache, brain fog, shortness of breath.

But if you take a look at this study, which was one of the earlier study to really look at this topic, it's a MET analysis and systematic review. It included about 21 studies from different parts of the world, from Asia, Europe and also the United States. Two things is obvious that if you look, what they have done, they looked at symptoms and then they look at lab of abnormalities. If you look very closely, almost every organ system is affected by long COVID. The other thing that was really revealing about this study is that there are about 50,000 people ages 17 to 87 and all the people that were examined in this study, 80% of them had at least one symptoms. So acute COVID leaves its mark on a vast majority of people.

The other thing we are beginning to appreciate is that in addition to the symptoms, we do find evidence of objective abnormality, pathologic abnormalities in many of the organs, whether you're looking at the heart, the brain, the reproductive system, there's clear evidence of damage to this organ associated with long COVID. We now know also that this is not a homogeneous entity. This is data from RECOVER Electronic Health, the N3C Consortium, that this clinical spectrum of disease is heterogeneous, the different phenotype, different subtypes. There's no one size fits all with this condition.

We don't fully appreciate yet what the impact of this condition is, but we know that the health and the economic impact is likely to be huge. Again, this is data from CDC looking at people with long COVID over time, about at least 25 to 30% of people claim that over time their symptoms lead to limitation of activities and in some of the cases it led to death. So this is a condition that has impact. And how this affect us economically, the impact on work, impact on different activities of life is, where the economic impact is something that we're still trying to understand, so this is not a condition that we can't afford to ignore. Then when you think about the disease trajectory, so what is unique about this study that was done about two years ago was that they not only look at symptoms, they look at symptoms at baseline and then a year later, but they look at the impact of the symptoms on the quality of life, personal activities, professional activities, social activities, morale, family, relationship with caregiver, unacceptable disease state.

We'll find out that even a year later after people have had their acute episode of COVID, the symptoms persist and these symptoms had impact on the quality of life. So what this tell us is that it's not going away. We are in this for the long haul. And there is no shortage of hypothesis or theory for the mechanism or the pathobiology of long COVID from viral persistence, immune dysregulation, the list goes on and on to autonomic dysfunction, and so these are some of the things we're beginning, many of us on this audience are working on. A lot of great studies out there, but many of them have limitation. Retrospective in design rely on electronic health record or electronic cohort. The population was impacted is not adequately represented. Many rely on self reports, small sample size and sometimes single site when there are multiple site, there are just a few three or four or five sites, and the follow-up period is limited, and the definition of long COVID is inconsistent.

So this is really some of the gaps. The promise of RECOVER, some of the gap that RECOVER is well positioned to begin to address. So what is the design of the adult cohort, the aim of the adult cohort? To characterize the incidents and the prevalence of this condition, to characterize the clinical cause and recovery, and to define the pathophysiology and the biological mechanism. In simple plain language it means, how many people are getting long COVID and why do some people get it and others don't get it? What type of symptoms do people present with when they have long COVID, how long do they get sick and why does long COVID happen at all? So the ultimate goal is really to first all figure out a way to accurately diagnose this condition, determine its severity, and then find a way to either treat it or prevent it.

So this is the timeline of recover, at least for the adult cohort. 2021, early part of 2021, the funding announcement was released. People applied and then the hubs and the clinical, the calls that were responsible for administering RECOVER was assembled within the first half of 2021. Also, during that time, the protocol was developed, and by October of 29th we enrolled a first participant at UT San Antonio. A little over about 18 months later, we had recruited enough to be able to publish the first two paper one and PLOS ONE and the other in

GEMMA. And by October 31 of last year, 2023, the adult cohort was completely enrolled and again the last patients were enrolled at UT San Antonio. So where are we? What is the scorecard? I just want to pause here that many of us who are involved with RECOVER will appreciate the complexity.

To say the study is complex is an understatement, whether you are involving it from the side of the funding agency, NIH as a participant, as a coordinator or scientist, every part of this study it's really complex. We wake up thinking about RECOVER, we continue the day thinking about RECOVER, and we go to bed dreaming about RECOVER. So what is the design of the adult cohort? So we recruited both COVID infected individuals as well as uninfected control, both during the acute and the post-acute phase, and then we followed them over a period of time, collected data prospectively and also collected data retrospectively. So it was described as ambidirectional longitudinal meta-cohort.

And these are the procedures. They were in tiers. So you have tier one procedure, which we basically have biospecimen minimal exams that everybody participate in, and then we have Tier 2 and Tier 3 that were administered to selected participants. These are examples of some of the Tier 1 procedure, just questionnaire, demographics, social demographic, social determinants of health, medical history, COVID history, vaccination status, minimal physical exam as well as basic lab. These are the symptoms that we looked at, 44 symptoms across the various organ systems in the body. These are some of the Tier 2 and Tier 3 tests, Tier 2 and Tier 3 tests, Tier 2 tests, and then Tier 3 tests mostly more advanced procedures such as biopsy, EMG, brain MRI, cardiac catheterization, gastric emptying study, on and on and on.

Today, when we closed enrollment in October, we had enrolled almost 15,000 people, to be precise, 14,779. 83% of them were COVID infected, 17% were uninfected control. They're from all over the country, 33 states and 83 sites across the country including Puerto Rico and DC. If you look at the demographic composition of those enrolled, it's a mirror image. You could not have a more representative population, particularly the population that were most impacted. Black and brown people were adequately represented in the cohort. So this is the volume of tests that have been done so far, 81,000 survey symptoms survey, 36,000 blood specimen, 1.9 million laboratory values, on and on and on. And here are some other examples of procedures and tests that have been done. So in a snapshot, this is where we are with the adult cohort. 83 sites from 83 states, almost 15,000 participants.

Millions of tests and procedure over 120 million data points. It's one of the largest most comprehensive of its type, representative pan-US prospective cohort, inclusive of the population group most impacted by COVID-19. So what is this data telling us? First and foremost, we gauge the temperature of the participant in the study, and what we're hearing from the participant is that they are with us, the participant and the community they represent, they are with us. And this means a lot to us that there are this participant who are investing a lot of the time. One of the unique aspect of RECOVER that you'll hear later from Brittany Taylor is really the engagement of our community. One of our participants, these are some of the assets from our participant. So this appeared to be a very well-planned and executed research study. I very much appreciate the time and the care that this study is researching.

Another participants said, "This is my first time being personally involved in a research project and I adore this research team. They are caring, instructive, educational and make me laugh to put me to ease. I understand how important this research is and how necessary it is to expand our knowledge of COVID and hopefully the nature of future viruses to protect future generation. I'm proud to be part of this study and I'll be sad when it is over." So with the data also we're beginning to define long COVID, we're starting first with symptoms. Many of you are familiar with this first GEMMA paper. Of the 41st symptoms that were evaluated, 37 across multiple pathophysiologic domain were identify as being more common six months or more following an acute COVID infection with an odd ratio of greater than 1.5, of these we have differentiate dose with long COVID.

This is a beginning, this is not the end of it, but we're beginning to objectively define this condition and what I just wanted to draw our attention to on this slide is the publication metrics of the dimensional batch. The study was published in June of last year. Within a period of six months, 125 citation, over 5,000 news measure in the autometrics at close to 200,000 view and 30,000 PDF download. So people are listening to RECOVER. So what is in the pipeline? We finished recruitment now the focus is on retention. We're trying to keep all of the 15,000 people in the study and we're also focusing on protocol fidelity implementation to do all of those procedures, the Tier 2 procedures, the Tier 3 procedure. We've begun to write papers.

There are currently 15 papers in the pipeline, and many more are on the drawing board, and before the end of this year you will hear more about the outcome, what is data from these 15,000 people are telling us. What are we looking at? We're looking at impact of long COVID on men and women, impact of long COVID across the lifespan, impact of long COVID on different groups about different demographic information, the laboratory abnormalities. There are over 40 independent mechanistic study including very detailed [inaudible 00:19:12] that are in the works that will help us really define the mechanism of disease so as to guide us to be able to provide accurate diagnosis as well as fashion appropriate treatment for this condition. So we've really developed one of the most elaborate infrastructure to address this condition. It's large, it is comprehensive, most comprehensive of its type. We have robust curated biospecimen linked with an elaborate amount of data. We've engaged some of the leading scientists across the US with diverse expertise. The study design is pragmatic.

We've enrolled the population group that are most impacted by this study. The data is beginning to offer an objective definition of the condition with a reasonable degree of precision. So what we need now is time. We need the continuing support of our community to deliver on the promise of RECOVER. I strongly believe that we are well positioned, we are poised to finish very strong. So with that I want to thank our participant and their community for their support of the study so far. I also want to acknowledge all of the hubs. There are 14 of them in the course, four of them that are involved in this study. And this hubs and code represent 83 different sites across the country, and we also want to acknowledge and thank our founder, the NIH, particularly the group from NHLBI for their support of this study. Thank you.

### Dr. Melissa Stockwell:

Thank you so much. It's my pleasure to tell you a little bit about the pediatric cohort and where we are and where we are heading. Thank you. Next slide. I'm going to review some challenges in researching long COVID in children, adolescents, and young adults. Talk about some progress to date and then some of our pipeline initiatives. So most of what we know about long COVID is from adults, and my colleague explained very well what is known and what is still to be discovered. And we really don't know a lot about long COVID in children or young adults, and there are really more questions than answers. There are a number of analyses or meta-analyses or studies that show a very high variability of prevalence from two to 70% of kids who have been infected having some kind of long-term symptoms.

And while we don't yet know the exact prevalence, even if we're at the low end of that spectrum, at two to 10% that is 1.4 million children in the United States who could be affected by long COVID and those children's lives may be affected forever, and so we really feel the absolute need that we understand what is happening. Next slide. We also know that there are a lot of other ways that children have been affected over the last, almost four years now, during the pandemic. There's a lot of stress for themselves and their family, changes in the economy, reduced physical play and social isolation and social anxiety, particularly starting early in the pandemic, and continuing really incredibly large educational losses, and disruption and growing autonomy and independence that we would expect children to move through every year as they get older, and just an extraordinary effect on mental wellbeing. And it's important that we understand both the infection itself as well as how all these things could contribute to risk factors for developing long COVID as well as the trajectory for recovery. Next slide.

There are a number of challenges in trying to understand long COVID in a pediatric population. There can be inconsistent manifestations of symptoms. We know that assessments of conditions and symptoms could be dependent on developmental stages, and for those young children it may be hard for them to describe the symptoms or if their parents are reporting for them to really understand what might be going on with them. There also are limitations of prior research similar to what was outlined for the adult cohort. Some of issues with study design, many are retrospective and lack control groups. Others may lack a standardized definition across studies, there can be different time varying from infection, small sample sizes or non-representative samples, different kinds of biases, limited or no follow-up. Many studies are looking only at symptoms, and many studies are either only single site or very few limited multi-site studies. Next slide.

So what are aims for the pediatric cohort? We are characterizing the prevalence and incidences of new onset or worsening symptoms related to PASC. We want to characterize the spectrum of clinical symptoms and including distinct phenotypes and understand the clinical course and recovery, identifying risk and resiliency factors for both developing PASC as well as recovery, and define the pathophysiology of PASC and identifying

biological mechanisms. Next slide. We want to understand how many children are getting long COVID. Why do some children get long COVID and others don't? What symptoms do children feel when they get long COVID? How long do children feel sick when they do get long COVID? What causes long COVID to happen? And really importantly, how does having long COVID affect later physical health, mental health and development in children really taking a life course perspective. Next slide.

Because we are pediatricians and adolescent medicine doctors, it's really important for us understand the impact of long COVID on families. This is an illustrative of quote of what families are really struggling with, "My daughter had COVID in December 2022 and months later she's really struggling. She's been out of school for six weeks with debilitating fatigue, pain and brain fog, none of which show any sign of letting up. All in all, COVID has been a devastatingly difficult journey for my family, and it's not one I wish on anyone." And it's important for us that we really understand how long COVID is affecting families in all age groups, so we're really looking at infants all the way up to age 25 and really centering ourselves on this experience of families, of children and adolescents with long COVID. Next slide.

The RECOVER-Pediatric Study population includes participants within four cohort types. There's the main cohort which is from infancy through age 25, and we're looking at acute cases of those who have been infected within the last 30 days, post-acute cases, uninfected, as well as enrolling caregivers to understand their experiences. There's also the ABCD cohort, an existent cohort, Adolescent Brain Cognitive Development cohort, which is focusing on adolescents 12 to 17 years of age, and many of them have enrolled in RECOVER as well, and we are drawing post-acute cases on infected cases as well as caregivers. We have a congenital exposure cohort focused on infants less than three years of age, including infants, both who were born with mothers who had COVID during pregnancy as well as infants who are not exposed during pregnancy. And finally we have our MIS-C cohort or multisystem inflammatory syndrome in children cohort was also an existing cohort of a newborn to 25 years of age who many are enrolling in RECOVER as well. Next slide.

Overall we have 103 enrolling sites for pediatric sites for RECOVER. Next slide. If we look at our timeline, we began enrollment a little bit after the adult cohort, so in March 2022, we met our primary enrollment target for our first phase for the pediatric main cohort this past November and we expect to end enrollment for special populations this coming May. Next slide. Similar to the adult cohort, we have a tiered study. So in Tier 1 it's remote where families and patients, if they're old enough, answer survey questions and have a remote collection of blood and saliva, then some group will move into this Tier 2, have more symptom questions and come in for a visit, for a checkup, have some blood, lung and breathing tests as well as EKG. And then our third tier is where a much smaller group of children and adolescents and young adults will be coming in for more intensive testing. Next slide.

Just to break down the different four cohorts that I mentioned, looking first at the pediatric main cohort, we have the pooled group which includes all the cohorts who are completing baseline Tier 1 as well as a smaller group of those who are acutely infected, and then about 6,000 of those will move into Tier 2. These are the in-person visits. Again, those are happening at 6, 12, 24 and 36 months, and then a smaller group will then continue into this deep phenotyping in Tier 3. Next slide. Our ABCD cohorts is primarily taking... It's really Tier 1 where they're completing surveys and blood tests, and that provides a really important opportunity for us to understand long COVID effect on the neurocognitive outcomes, particularly among adolescents, and so we are very fortunate to be able to run the study alongside ABCD. Next slide.

Our congenitally exposed infant cohort has two of the tiers. So again that same baseline Tier 1 and then all of those infants then enroll and continue on to follow up in Tier 2 with a focus really on neurocognitive and neuro development as well as growth, really understanding how potentially the effect of infection during pregnancy. Next slide. And finally our MUSIC cohort, which is the extent cohorts affecting [inaudible 00:29:33], studying multisystem inflammatory syndrome in children. Those who are enrolled in MUSIC are doing a modified version of Tier 1, 2 and 3 including the longitudinal data collection. And they also have previously collected data from closer to when they were affected with MIS-C. And so this really allows us to put those data together and really begin to understand long-term impacts of MIS-C. Next slide.

So just to briefly look at some of the key procedures for Tier 1, these are the questionnaires, obviously demographics and [inaudible 00:30:10] global health assessments, understanding about infection, symptoms. But then also importantly, what are some of the health consequences, so diet, physical activity, sleep, impact on school and a lot of information about potential social determinants of health. Our blood specimens for tier one are

remotely collected at home. We are collecting both on the child and as well as the caregiver if they're enrolling themselves and saliva collection on the child caregiver as well as the other biological parent if they are enrolled. Next slide.

Some of these symptoms will look familiar to the adult cohort, but because we know less about the pediatric long COVID in children, adolescents and young adults, you can see that we have a very long wide variety of symptoms that we are collecting over 70 of them, and you can see they're among different organ systems here. Next slide. For our assessments, Tier 2 onsite assessment, we are collecting height and weight and vital signs. You can see here we're doing a 10-minute standing test for assessing for dysautonomia, a flexibility score, EKG, spirometry, neurocognitive and testing, as well as assessment of emotional development, clinical labs as well as biospecimens. And for our Tier 3 with our more intensive testing that includes echocardiogram, cardiac MRI, cardiopulmonary exercise testing, PFT, sputum induction, and then brain MRI and EEG, as well as more further in depth assessments both for neurocognitive assessment and emotional development as well as impact, as well as cognitive biospecimens. Next slide.

So where are we so far? Overall for our participants, we have enrolled over 14,500 participants and that includes those who are acutely infected, infected, post-acute, uninfected, as well as congenital cohort. We also have enrolled over 7,600 caregivers, which brings our total enrollment so far to over 22,000 people. Next slide. The demographics of our participants also is reflective of the national demographics. As you can see here with about 4% American Indian and Alaska Native, Native Hawaiian, Pacific Islander, 8% Asian, 14% black, 27% Hispanic, 57% white and 1% who felt that these categories didn't describe them fully. Just to note, these are not mutually exclusive groups since people could self-identify in multiple categories. Next slide.

Our main cohort does age in the range of zero to 25 and we have good representation in each age group. As you can imagine, we have a larger number of those who are adolescent given the collaboration with ABCD, and 31% of our families come from medically underserved area. Next slide. Overall in terms of what we have, we have a large amount of data we have collected to date. We have collected over 14,000 symptom surveys. We've had 15,000 blood biospecimens banked. We over 15,000 laboratory values, 1100 Beighton tests for flexibility, a thousand active standing tests. And actually it's interesting aside, one of our patient representatives told us this may actually ultimately be the largest cohort where we are doing active standing tests in adolescents, which would maybe be actually important beyond just for recovering for long COVID, but to understand what might be the norms for active standing. We have over 1300 electrocardiograms, 1100 spirometry tests and over 1100 cognitive evaluations. Next slide.

So what's in our pipeline? We are very eager to start our Tier 3 testing and just putting all of those last pieces in place as well as beginning to publish some of the data. This is a focus particularly on the pediatric main cohort. Our first paper is characterizing the post-acute sequelae or PASC in children that will allow us then to identify some clinical risk factors for PASC in children, identifying social determinants of health that might be associated with PASC, and then it's a paper looking at the prevalence and natural history of antibodies in children and associations with PASC. Next slide.

So in conclusion, the RECOVER-Pediatric cohort is really poised to address very key long COVID research questions in children adolescents that we think are still unanswered. Uniquely, we have perspective collection of data, biospecimens and imaging across the early lifespan, so from infants to young adults, and we do expect to have findings that do differ from the adult cohort as well as differ among age groups within the pediatric cohort. We feel we've got a very exciting year ahead of us and look forward to being able to return in the future to share some of our data. Next slide. We really would like to acknowledge and thank all participants and their families who really are just so generous with their time, our study sites and staff, all our [inaudible 00:35:32] representatives and patient caregiver and community, our governance and scientific committee representatives. This does take a village, it's a very large and complex study, so we are very fortunate to have so many sites as our lead sites, the ABCD, MUSIC as well as all of the core sites, and are very grateful for NIH for this funding. Thank you.

## Dr. James Stone:

Hello. I'm James Stone and I am the chair of the RECOVER Autopsy Cohort Coordinating Committee, and I'm very happy to be able to talk to you today about what we're doing to try to understand and gain more and

more complete understanding of this chronic debilitating condition that many of you are suffering from. Next slide please. So why autopsy and why do we think this is going to add a very important component to our understanding? Well what autopsy actually allows you to do is to directly assess for tissue changes with very highly sensitive approaches. This is in contrast to serum studies which really are somewhat indirect where you're trying to infer which organs are involved and what's happening within the organs. And what we're doing with the autopsy tissue is much more sensitive in terms of finding changes than you could do for example with imaging or even with biopsies which are very often of small amounts of tissue.

So what we're getting at here is that with autopsy you can obtain these very difficult to obtain tissues like the brain, the heart, and even other organs in relatively large quantities, and this allows us to do very thorough analysis to understand not only what the virus is doing, if the virus is there, but how is the host responding? Are there other factors beyond virus that we need to be paying attention to that haven't yet come to light? So this is why the autopsy study is so important. But more importantly with autopsy you can simultaneously analyze multiple organs throughout the body. When you're trying to look at biopsy studies, you might see a pathologic change or some sorts of change in the tissue, but you really don't know with just the biopsy if that change is a primary part of the disease or if that's really a change that's secondary to some other organ being influenced in the body, and with autopsy you can analyze the organ simultaneously throughout the body.

Importantly for the RECOVER Autopsy cohort, we have designed this study in order to obtain high quality tissue that is suitable for use with modern advanced experimental approaches including all omics technologies. This is really in contrast to standard retrospective autopsy cohorts that often does not utilize tissue nearly as high a quality as what we're going to be using here with the Autopsy Cohort in RECOVER, so this is why autopsy will play such an important role as we move forward with the studies of this cohort and consortium. Next slide please.

So this is the timeline for the autopsy cohort and it's a slightly different timeline than you've been hearing about for the other cohorts. We did have the same initial ROA release in February of 2021 and our hubs were selected by July of that year, so around two and a half years ago. We'd had to complete a very detailed autopsy protocol, which took time and also the cores had to be established for us to start the autopsy procedures. The protocol and the course were completed by January and we were able to start enrolling in March of 2022. However, unlike the other cohorts, this is a four-year enrolling process for autopsy, so we're not even halfway through the enrolling process, so we're still in the midst of active enrolling with autopsy. We did publish our protocol paper in PLOS ONE that details our autopsy protocol, so that's open access so everyone can access that and read exactly the details about what we're trying to do. Next slide.

So these are our enrolling hubs for the autopsy site. We have four sites that are hub sites that also enroll. That's the University of New Mexico, Mount Sinai in New York, Massachusetts General Hospital in Boston and the Mayo Clinic in Minnesota. We do have a hub site which is not itself an enrolling hub site CVPPath Institute, but it oversees the activities of two subsite which enroll, that's New York University and Howard University. Next slide. So many people might initially think that most of our activity, the bulk of our time is spent doing autopsies for this cohort, it's actually not. It's actually screening and enrolling. We do a lot of screening and this involves basically at each enrolling site, the decedents at those institutions, anyone who dies at those institutions or in those hospital networks are screened for eligibility and suitability for the project.

We basically identify the decedents who meet enrollment criteria, which primarily are known or suspected SARS-CoV-2 infection and they have to be dying at least 15 days or longer from initial infection in order to make it into one of our patient categories. So we then obtain the autopsy permission and the RECOVER Study permission from the next of kin after the patient has died. So far over 20,000 deceased patients have been screened to date, so this is a large amount of screening going on to identify the proper cases so we can shed as much light on this condition as possible.

Next slide please. So just so everyone knows the definitions, we use slightly different definitions in the autopsy setting for what we're defining as PASC is the presence of any new symptom or significant worsening of a preexisting symptom that's not due to a cause that's independent of a PASC related process, and it must last for at least 60 days following the initial infection. By something that's independent of a PASC related process, we're talking about situations such as trauma. So obviously if an individual has trauma after having COVID and has pain because of that, that would not qualify. But we've kept this definition very broad because we want to try to

capture all the different types of people who are suffering from PASC, even if their symptom may be an uncommon one and may not be one of the ones that were top on the list that you saw earlier.

The post-acute PASC negative patients would be similar at least 60 days following infection but without new symptoms. And for us, we're defining our acute phase patients as those dying 15 to 59 days after the initial infection. This really is the acute phase and to somewhat the extended acute phase. We want those patients to have lived at least 15 days so that there are some early changes in the organs and we can compare those then to the patients who are actually suffering from PASC would be the reason why we're not enrolling the patients less than 15 days. Go to the next slide please.

So this demonstrates our sampling when we do have our autopsies. We're sampling 55 anatomic tissue sites throughout the body. This is a large amount of sampling. These are not standard routine autopsies. This is extensive sampling. If you look at the top on the right, you can see in those top three columns all of the different sites from the brain that we are sampling. As you move around clockwise, you see the heart sampling with multiple sites throughout the heart, also the spleen, multiple sites through the gastrointestinal tract, the pancreas, the ovary, the testes, transplanted organs if there are transplanted organs. Importantly at the bottom we are sampling peripheral nervous system, the peroneal sural nerves, so peripheral nerves as well as ganglia, both sympathetic chain and dorsal root ganglia. And I think it's important we have included so much neuro sampling in this protocol because of the prevalence of neurologic symptoms in many of the patients with PASC.

As we move up, you can see we're also doing skin and subcutaneous tissue, skeletal muscle sampling, kidney adrenal glands, the liver, bone marrow. And of course, as we get up towards the top on the left, we're extensively sampling lung tissue as well. So we're sampling tissue for this study throughout the body to try to understand what's going on in patients not only with PASC but with different forms of PASC. Now, a key component of this study is that we require a postmortem interval of less than 24 hours. This is far different than a standard autopsy, probably the average autopsy, the postmortem interval is more in the range of two to three days, not less than one day. This allows us to have very high quality tissue that we can use in research protocols. Also, we minimize or we strictly control the formal and fixation time between 16 to 32 hours. This helps to prevent RNA degradation as well and maintain the high quality of the tissue, and that's for the tissue that goes into eventually becoming paraffin blocks.

Go to the next slide. So on the far left, for each of those 55 sites, we have two pieces of frozen tissue and one piece of paraffin embedded tissue. But in addition to that we also have CSF fluid, the fluid that's around the brain and the spinal cord. We also have serum, blood spot cards, bronchial swabs and stool. And all of this material goes to a biorepository, which is at the Mayo Clinic, and that biorepository will make histologic slides from the paraffin block. Those slides are scanned with whole slide imaging and they actually become part of a digital slide archive that the investigators are using to look at the histology, and the specimens are stored there for studies then to be performed. And all of this specimen acquisition is being overseen by our Clinical Science Core, which is at New York University. Next slide please.

So there's autopsy cohort data being generated as well. We carefully record the pre-mortem clinical data, the demographics of the patients, the PASC medical history, their medications. As treatment trials are underway, we will be recording whether they are on treatments potentially for PASC and how those may or may not affect the tissue changes that we're seeing in the autopsy. We also look at pre infection, laboratory tests, imaging results, COVID symptoms of course, any tests, treatments, vaccinations are important to record to see how that's affecting what we're seeing in the tissues, and any re infections we carefully record and, of course, the PASC symptoms. There's also information that we store from the autopsy reports including both the gross and microscopic autopsy findings. All of this information is going into a red cap database which is accessed by our researchers. And this is managed by our Data Resource Core, which is at Massachusetts General Hospital. Next slide please.

So everything I've talked about so far regards our Tier 1 patients it's what happens to all of the autopsies. For half of the cases, we also do ex-vivo hemibrain MRI, meaning we're doing MRI analysis on half of the brain. The reason it's half of the brain is because we need to sample the other half afresh. So we have to cut half of the brain fresh to take the samples for the study, but then the other half we can scan using an MRI device. And this is often a much higher resolution than you can see in vivo with a live person because there's less motion artifact, and this is a protocol that is run at 3 Tesla magnet strength for one hour. We upload these scans into an AMBRA system, which again allows the scans to be read by multiple sites to interpret the changes. And we're eager to see how these MRI



changes correlate with some of the histologic changes that we're seeing, for example in the other half of the brain. Next slide.

So this is where we stand with our autopsy enrollment. We've enrolled 186 autopsies so far. 36 of these are PASC patients, 122 are post-acute PASC negative and 28 acute patients. In all there's over 8,000 anatomic tissue sites have been acquired and stored in the biorepository. Next slide. So in terms of demographics, I feel that we're doing very well with the autopsy cohort. When you look at the American Indian Alaskan Natives, Native Hawaiian or other Pacific Islanders as a group, we're actually enrolling at a rate higher than the US population. Also with the Middle Eastern North African group along with the Black or African-American and Hispanic groups, we're on target with the US population. With Asians, we clearly are not and that really relates to different cultural and religious issues concerning autopsies in that particular group. However, we're still actively trying to enroll Asians. They're certainly not excluded from the group.

Also, in addition to continuing to try to enroll Asians into the autopsy cohort, we do want to increase our Black or African-American enrollment because that group was disproportionately affected by long COVID. So we want to try to increase that beyond the rates in the US adult population. Next slide. So right now there are multiple ongoing autopsy cohort studies. There's Pathologic studies, Imaging correlation studies and Mechanistic Omic studies that this tissue in these samples that we're collecting will play a very important role in helping us to understand what's going on. Next slide. So in conclusion, the autopsy cohort is currently enrolling a diverse population of decedents. The tissue is an invaluable resource that offers unique opportunities to elucidate the mysteries of PASC and it's a very high quality the tissue and will be utilized in multiple ongoing and future studies. Thank you.

### Brittany Taylor:

So I am Brittany Taylor. I'll be sharing some insight on the role of representatives with RECOVER. So here is an overview depicting components of RECOVER. You'll see at the top our governing committees and other components which included our protocol working groups, writing groups, and the governance and scientific committees in conjunction with the National Community Engagement Group. Representatives are placed on all of these committees as we believe it's important that there is representative voice and insight provided since this is the largest and most diverse patient-centered study on long COVID. So who are representatives? In short representatives are individuals with lived experiences on COVID-19 and or long COVID, and here you'll see a more outlined depiction of what that means. So patients either have long COVID and are COVID-19 survivors. The second category of representatives are caregivers, so they have a family member or a close friend with long COVID that they are taking care of. And then we also have community representatives, so these are individuals that live or work in communities where COVID has affected a large number of people or it's just overburdened by COVID and long COVID.

We also have representatives that just want to share their personal experiences and help inform and shape the future of RECOVER. So what does the representative representation look like? We are predominantly patients, and about 44 patient representatives followed by 16 community members and then eight caregivers. It's also important to note that representatives are not mutually exclusive. You'll also see the geographic distribution of representatives with the East Coast bearing the majority of representatives. The Northeast having the highest number followed by the southeast, and our lowest representation is in the Midwest. I myself serve as a community member and I am located in Atlanta, Georgia. When you look at the demographics of representatives, this is how we are representative with the majority of White individuals followed by Black or African-American. We have about five Hispanic Latino representatives or Asians. We did have one that preferred not to disclose, and there you'll see a White American Indian, Latino-American Indian and Black or African-American and American Indian.

Our breakdown by observational cohort, the bulk of representatives do sit in the adult cohort followed by the pediatric cohort and then autopsy. So the guiding group of representatives is called the National Community Engagement Group and we also call ourselves in NCEG for short. The National Community Engagement Group provides leadership and promotes meaningful discussion, genuine partnership and shared decision-making across RECOVER. You can think of that as meaning, we integrate principles of community engagement to enriched science, elevate patient experiences, and ensure promotion of health equity across RECOVER. We are doing this through four subcommittees that we have created and that is the publication subcommittee, which is used to

ensure that representatives are on RECOVER manuscripts, important to have us included in the science that's being published. We also have a Communication Subcommittee which ensures that we're sharing information to representatives in a form that's understandable. We have our representative engagement subcommittee, which helps to build community and collaborations across the representative body for RECOVER. And lastly, we have the Health Equity Subcommittee, which is a newly formed subcommittee to ensure that we are making a concerted effort to address and integrate health equity across RECOVER.

So here is a snapshot. We wanted to create an image that depicted how representatives are contributing to RECOVER. Here you'll see that we have learning hubs, so these you can think of as webinars that share information. We address different topics that are important to representatives in the science in addition to long COVID. We use our communication platform, which is predominantly Microsoft Teams where we post questions, ideas, share information, and create documents. We also have local engagement. So representatives sit on various committees within their community, also are represented on the local sites. There are over 200 sites for RECOVER, and so it's important for us to be engaged at the community level and at the site level to discuss information about long COVID and reach communities affected most by COVID and long COVID. And we also publish a newsletter.

This newsletter helps to highlight different things that are evolving and ongoing across recover, including accomplishments and study findings, breaking news and upcoming events that are important to our long COVID community. So in the center you'll see that representatives are, of course, represented by patient, caregiver and community representatives who are either a representative at large or sit on the National Community Engagement Group and serve on coordinating committees. The NCEG is a smaller group, so there's a total of 17 NCEG members, whereas the larger group represents about 68 representatives across RECOVERs. The demographics here are a bit different. So 53% majority African-American, followed by White with 24%, Hispanic, Latino, American Indian, Hispanic, Latino and then the multiple races. When you look at the cohorts, we're predominantly located in the adult cohort with only 6% distributed in the pediatric cohort. And then if you take a look at the type of representatives, the majority again are patients as you saw with the larger representative body followed by advocacy group members.

And then community members. And we also have representation from scientists, caregivers, and then we do have some reps who identify as both a caregiver and a patient because they're caring for themselves in addition to family members and friends. And you'll also see for our educational level, the large majority of us do have some form of postgraduate or professional degree followed by those with a college degree. And this information is provided based on how we indicated when we enrolled as a RECOVER representative. Here I want to highlight the representative contributions to recover. So beginning in 2021, we helped create study plans. We drafted and reorganized the COVID symptom survey. We updated inclusion criteria to ensure that people who had COVID prior to the launch of RECOVER could join. And we added more questions to the participant survey and provided feedback on materials that are used to recruit patients and representatives. In 2022, we supported extending the inclusion criteria from 12 months to 36 months. We helped create a participant feedback questionnaire to assess how we are feeling as patients and participants of RECOVER. We made modifications to the adult Comorbidities Case Report form.

We assisted with creating a video that showcased the impact of RECOVER from the representative and patient vantage point, and we began hosting learning hubs for representatives. In 2023, we evolved a bit more and we started partnering with researchers to share study findings via publications. We advocated to extend the enrollment period for diverse populations to increase patient diversity. We organized a White House long COVID council representative briefing with HHS. We've routed caregiver and disability insight to improve autopsy recruitment. Representatives began serving as panelists for these R3 seminars. We developed authorship training for representatives and researchers to ensure that researchers understood what it meant to have representatives participate as part of the manuscript and publication process. And then we developed and launched NCEG subcommittees and the representative newsletter. I did want to take an opportunity to highlight the NCEG impact. So as a part of NCEG, we co-design marketing materials for diverse recruitment, so we ensure that these materials were specific to the Native American populations, Hispanic Latino populations, and the African-American populations to increase and diversify the patient population. We enhance patient and representative recruitment, so we work to drive up those enrollment numbers.

We revise the authorship guidelines. So guidelines were already in place, but the NCEG co-chairs revise those authorship guidelines better defining the levels of involvement of representatives in addition to the payment for representatives who contributed to authorships. We promoted plain language incorporation, and you can see that evidence in the R3 seminar descriptions. We also ensure that plain language was incorporated in the manuscript descriptions that are released to representatives when we're requesting representation from us in the writing process. We expanded representative voting power. So we wanted to ensure that not only did representatives participate on these various committees, we wanted to ensure that our voices counted and that we had an opportunity to vote on these guiding principles and decisions being made that impact the cover.

We served as reviewers for clinical trial research opportunity announcements. We were able to amend the scope of manuscripts so we did have an opportunity to flag and change and correct the course of some manuscripts. And in addition to that, we do have some representatives that are leading manuscripts for RECOVER. We work with NIH to guide community engagement restructuring and we have amplified and continue to amplify patient and representative impact across the study. Some challenges that we experienced from the representative standpoint was to develop a comprehensive feedback mechanism for bi-directional communication. So ensuring that things discussed at the top did reach us as representatives even if we were not present in all of the rooms. We were initially met with the challenge, ensuring diverse representation. We'll talk about demographics of the researchers. We also want to talk about the demographics and representation of representatives as we did display an over-representation of the adult cohort, and we're still trying to recruit more individuals for the pediatric and autopsy cohort.

We did notice a slow acclimation to the community engaged approach as it did launch a little bit later than the initial RECOVER launch. We have experienced siloed cohorts when you want to compare observational cohort and the clinical trial cohort, and the delayed communication or sometimes less than desired communication between the two cohorts. And then the rapid nature of RECOVER sometimes left us working on materials and information, but due to the pivots and the rapidly releasing science on long COVID, some of those came void before they were actually released.

So where are we now? As representatives, we are integrating a health equity lens across RECOVER. So just making sure we're integrating health equity across RECOVER observational and clinical trial cohorts. We are informing the mobile health platform revamp to make sure it is best serving our patients. We are assessing representative contributions and impact potential for the future, ensuring that we are best being served across RECOVER, and we are increasing awareness and informing research on long COVID for projects external to RECOVER. I'm going to talk about the future of RECOVER as representatives will continue to inform RECOVER's future. We'll continue to expand membership across RECOVER as representation fluctuates. We'll continue to amplify health equity, and we'll continue integration of patients and representatives in RECOVER Clinical Trials. We do plan to launch some community engagement training modules for representatives, and we'll continue to strengthen the infrastructure for future patient and community engagement studies. And lastly, we will, of course, continue to participate as patients in RECOVER Clinical Trials.

And lastly, here are some points of interest that we are exploring for the future of representatives with RECOVER. Of note, health equity is always at the top, so our social determinants of health, clinical trials, the impacts of COVID on mental health and disability justice along with patient advocacy. And that almost concludes my presentation. I did want to thank the NCEG co-chairs, NCEG members and the representative body as a whole in addition to the NIH for ensuring that patients and representatives are integrated across RECOVER as a whole. And that will conclude my presentation.

### Claire Quiner:

Wonderful. Thank you, Ms. Taylor, as well as to the other panelists. I'd like to begin by asking some questions submitted from the audience prior to the presentations today, and then we'll get into some of the questions submitted throughout the course of the last hour. Since you just wrapped up, Ms. Taylor, I'd like to begin with you. Could you tell us how RECOVER has enhanced because of the representation, involvement that you just described?

### Brittany Taylor:

Sure. So ensuring that there are patients as a component of representatives in RECOVER, that allows an opportunity for the lived experiences to be heard in real time. It shed light on what patients and individuals that are experienced as a result of having long COVID and informed researchers or scientists, the leaders of RECOVER on things that they might not have otherwise been aware of. We are informing long COVID research with projects outside of RECOVER. You want to think about just last week with the US Senate hearing on long COVID where we had caregivers, representatives representing the RECOVER initiative and sharing their experiences and their insight and feedback on their experience thus far with RECOVER, but as a long COVID patient as well.

And we also contributed to the National Academies Symposium that took place last year where we shared experiences from the advocacy standpoint as a patient and also as caregivers, and that in turn is helping inform RECOVER. It helped also inform the process and launch of the clinical trial component of RECOVER. So I think being able to inform pretty much all facets of how long COVID affects patients and caregivers and the communities that have been disproportionately affected, it's helping to inform RECOVER as a whole.

**Claire Quiner:**

Wonderful, thank you. And just as a quick follow up, could you give some specific impacts that representative participation has had on recover?

**Brittany Taylor:**

So I think we can think about a small impact, so ensuring that representatives were aware of the ADA status where you can receive disability for having long COVID, not all representatives were aware of that, and as the NCEG we made sure to send that information out and point them in that direction. In conjunction with that we are... Sorry my light went out but I think you guys can still see me.

**Claire Quiner:**

We can, thanks.

**Brittany Taylor:**

We informed methods of information delivery and how it was a bit over burdensome in the beginning with the flow of information coming from RECOVER and the need to slow that down and better categorize that. And then just having patients continuously share their experiences with their providers and bringing that back to RECOVER to the researches and the leadership, and what that is looking like and how they're feeling has been critical to RECOVER.

**Claire Quiner:**

Wonderful, thank you. Switching gears a little bit, I want to open these questions up to the entire panel. Could someone jump in and describe how RECOVER infrastructure can be leveraged by other researchers?

**Dr. Ofotokun:**

If you don't mind, I can go ahead and start.

**Claire Quiner:**

Please do.

**Dr. Ofotokun:**

So the data that has been collected from what is almost, if you took the adult cohort of 15,000, pediatric cohort of more than 20,000, the autopsy cohort, it's a huge data. So these are history, social demographic data from the participant samples of all types, whatever you can think of, blood, peripheral blood smear, swab from the nose, salivas, to say tons and tons and tons of specimen and data that are linked. Perhaps, one [inaudible 01:15:07]

valuable asset for understanding the mechanism of disease, so all of this data is available to the public, to the researcher. And so there's a mechanism, there's what we'll call an Ancillary Study team that receive concept. It's a very simple process, a concept of no more than three to five pages. It's submitted to this group and they review it for the scientific value, and this committee include also patient representative and the community. And then once that review is done and usually it's a very fast process that takes less than two weeks, and it's approved, then a mechanism is set in place for you to assess either the data, the specimen or both<sup>1, 2</sup>.

**Claire Quiner:**

Wonderful thing. Thank you.

**Dr. Ofotokun:**

Thank you. There's a website which you can go to RECOVER, a website that describe this process.

**Claire Quiner:**

Wonderful. One other question that, perhaps, you could answer for us, Dr. Ofotokun, a number of audience questions today are about whether RECOVER is studying treatments. Could you or anyone else on the panel share some information about the clinical trial component of RECOVER and how the observational studies form the basis for those?

**Dr. Ofotokun:**

Thank you for asking that question and thank you for the audience members that have asked that question. And again, we've heard this again, this really emphasized the value of incorporating community and patient into RECOVER. We've heard from our community what they want and I think the desire of the community is the true north of the RECOVER Study. We want to find a way to diagnose the condition very accurately. We want to find a way to prevent it. We want to find a way to treat it, and so the observational cohort is really the beginning of that process, aggregating a lot of data that will help us to understand exactly what is long COVID, how do we diagnose it, how do we understand the severity, what type of long COVID do different people have? This information inform the type of clinical trials and treatment trials that we will be undertaking.

And the direct answer to that question is yes, clinical trials have started. There are several clinical trials that have started, at least three of them that I know of. The Vita, which is actually offering treatment. There's a Sleep Study that is offering another types of treatment. There's also the autonomic study and there are several others that are about to start that are really... A lot of the information that inform the design of these clinical trials come from the knowledge that is coming out of the Observational Study. And this is what we hear from our community, from our patients, our participants, that they need treatment, and this is why we do this. We do the observational studies not because we just want to observe people, we collect this data so that we know what type of treatment to design for this condition. And I think maybe one of the next seminars should focus on these clinical trials that are now currently ongoing to take care to treat patient with long COVID.

**Claire Quiner:**

Thank you. There's clearly interest in that area and what we know so far. I'd like to switch gears a little bit to talk more specifically about the details of the study data and findings. My first question are submitted from audience members are, "Are long COVID patients who've met diagnostic criteria for ME/CFS being tracked?"

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<sup>1</sup> RECOVER research data from the publication "[Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection](#)" are available as a de-identified datafile consistent with NIH data sharing policy. Individuals who would like to access the datafile must review the Data Use/Sharing Principles and Code of Conduct for the RECOVER Data Gateway and complete the [datafile request form](#). Once the form is complete, requests will be reviewed and additional information to obtain the data will be provided to requestors.

<sup>2</sup> NIH is also soliciting applications to support studies that use patient data and samples of bodily fluids (biospecimens) already collected by RECOVER researchers. Research proposals are due March 22, 2024. Applicants to this research opportunity announcement (ROA) must be investigators at research sites already supported by RECOVER. See the [ROA](#) and application requirements at [recoverCOVID.org](#).

**Dr. James Stone:**

We would certainly track that information within the autopsy cohort. I suspect that question was meant for the adult cohort.

**Dr. Ofotokun:**

Yes. The answer to that question is yes. So remember I said in my presentation that there are different phenotypes, different subtypes of long COVID. We are taking the pain to understand all of the different phenotypes, all of the different subtypes and strain, and this is also being carefully, tracked and I think we have a paper that is near done to really describe our findings in the adult cohort.

**Dr. Melissa Stockwell:**

Then just to add for the pediatric cohort, we have been updating our Tier 2 symptoms. So we had some of the symptoms related to ME/CFS, but to be also be making sure that we are adequately catching, particularly post-exertional malaise since that's something that obviously can affect everyone with long COVID, but particularly children as well, which can be very devastating, and making sure that we're adequately capturing that both in our Tier 2 and then also in our Tier 3 studies as well. So with those both together, and I did see another question just about MCAS, I just want to answer that as well. We also do have some questions and are actually adding more to really making sure that we are really capturing mast cell activation Syndrome, MCAS, in the pediatric cohort.

**Claire Quiner:**

Thank you. I did also want to share that I previously served on a committee that was supporting modifications of the protocol early on, and I do note that there were additional questions and parts of the protocol that were modified to ensure that the diagnostic survey for ME/CFS was being implemented more appropriately, so that is a subgroup that's being tracked and studied in addition to what the panelists have said.

**Dr. Melissa Stockwell:**

And just add to one more thing, just in terms of the patient representative, in all of the cohorts they're, in our case, parent representatives really are very much embedded into the coordinating committees and we actually get a lot of incredible information in terms of understanding how do we need to change the protocol, what our family's feeling, and really they are our eyes in the community as well as really active members of the protocol changes and as we are rolling out different phases, so very much what Brittany said, very much integrated into the protocols and into the coordinating committees.

**Claire Quiner:**

Wonderful. Here's a question for you, Dr. Stone. "Are you planning on studying small fiber nerves and skin and blood vessels? Are you planning on studying autonomic ganglia?"

**Dr. James Stone:**

Yes. All of those are being studied as part of the autopsy cohort. There's obviously ancillary studies going on outside of RECOVER on those issues as well, but certainly within the autopsy cohort those will be studied.

**Claire Quiner:**

Wonderful. And did you have any initial observations from the autopsy study to date?

**Dr. James Stone:**

We don't have observations to date that we can share at this point. It's still ongoing and we're very early in the process. And I know there were a lot of questions about four years of enrollment for autopsy, and the truth is fortunately most patients with PASC aren't dying quickly. So that's why it takes four years for us to get adequate

numbers of the right types of patients enrolled in the autopsy study. We want to be very careful, enroll the right types of patients so that we're able to adequately answer the questions for all the different forms of PASC that are out there.

**Claire Quiner:**

Wonderful. I think we have time for one final questions. I see a great one for DR. Ofotokun. "On the disease trajectory slide, the chart seems to show that symptoms reduce the QOL and the QOL initially improves, but symptoms increase and the disease burden begins to increase around 300 days post infection. Do you have any thoughts on what this means?"

**Dr. Ofotokun:**

Thank you so much for asking that question. What that paper seemed to describe, and this is what we see in real life situation, is that the disease condition waxes and wane, so there are times when people seem to improve and then it comes back again. When we think it's gone, it's not gone and we would hope it would go away, but the experience is that it goes up and down, and the duration, the lapse, we don't quite understand yet the gap between the fluctuation of the symptoms. What we're seeing in majority of our patients is that it waxes and wane, and a year later, majority of peoples have symptoms, not symptoms alone, but symptoms that are debilitating that affect their quality of life.

**Claire Quiner:**

Wonderful. Thank you. With that, I'd like to thank you all for your terrific presentations. We appreciate you sharing all of your time and expertise. A recording of today's seminar will be available on [recovercovid.org](https://recovercovid.org). That'll be available within several weeks. We'll also be posting a Q&A document that has responses to the questions we received today, including some that we did not have time to answer. This slide lists the topics for the upcoming seminar. We have an exciting topic and we hope to see you at future sessions. Additionally, you'll see a short survey come up on your screen. I believe it's there now. We'd love your feedback on this seminar and we'd appreciate if you could take a minute to fill out this brief survey. Thank you very much everyone, and have a great day.