

Transcript

Dr. Christine Bevc:

Hello and welcome. I'm Christine Bevc, Task Lead for RECOVER at the Administrative Coordinating Center and moderator for today's webinar. I'd like to welcome everybody to today's RECOVER Research Review or R3 webinar. The overarching goal of this webinar series is to catalyze the formation of scientific stakeholder community within and beyond the RECOVER consortium that's fostering a shared understanding of the state of science and providing educational resource to both RECOVER Investigators and the broader scientific community of clinicians, patients, and public stakeholders.

I want to start by thanking everyone who submitted questions in advance. We have those and we're hoping to get to as many of those as possible. During today's webinar, as Shane mentioned, please use the Q&A feature to submit those, and after the presentation today, our presenters are going to be answering as many of those as possible and providing responses in realtime within the Q&A. So you can check back and see if they've actually responded to your questions there. Please note that we will not be answering any questions about clinical care. Afterwards, the NFAQ document for this webinar is going to be posted along with the recording on recoverCOVID.org. Today's webinar is part of our ongoing series, RECOVER in Action. For today, we're focusing on the status of RECOVER clinical trial protocols. Our panel today will take us through the landscape of long COVID's clinical trials and the development of RECOVER's upcoming clinical trials if you haven't already remembered to sign up on the website to receive future announcements and updates for the series. As RECOVER continues to grow, we want to remind our audience the information presented in this seminar is intended to stimulate collaborative dialogue amongst the RECOVER scientific community, as well as study participants in other interested parties. In addition, our disclaimer, none of this information should be interpreted as medical advice.

So please join me in welcoming three members of the RECOVER Clinical Trials Team joining us today, and it's my pleasure to introduce Dr. Eldrin Lewis, Dr. Kanecia Zimmerman, and Ms. Renee Leverty. They're joined by our discussants, Christine Maughan and Marta Cerda, who will help kick off our discussion and response portion of our webinar. Also, we're joined by Dr. Hernandez from the DCRI Institute at Duke.

Our first presenter today is Dr. Eldrin Lewis. Dr. Lewis currently serves as the co-chair of the RECOVER Clinical Trials Steering Committee. He's also Chief of the Division of Cardiovascular Medicine and a professor of cardiovascular medicine at Stanford University. Dr. Lewis is going to introduce us to the landscape of long COVID trials and the RECOVER's progress to date.

Then next, we're going to hear from Dr. Kanecia Zimmerman. Dr. Zimmerman is the PI, Principal Investigator of the RECOVER Clinical Trials Data Coordinating Center, CTDC, at DCRI, which stands for the Duke Clinical Research Institute at Duke University. Dr. Zimmerman will share more information on the overview and status of the planned clinical trials.

Then we're going to wrap things up and hear from Ms. Renee Leverty, who will talk us through about the inclusion of patient representatives throughout the clinical trials development process. Ms. Leverty is the Engagement Lead for the RECOVER Clinical Trials, and also serves as the Program Lead for Stakeholder Engagement at the Duke Clinical Research Institute.

Our panelists are also joined by two of our RECOVER patient representatives. I mentioned them, Christine Maughan and Marta Cerda, and they're going to help lead off our discussion with a short series of questions for our panelists, as well as speaking to some of their experiences. So following those questions, we're going to open the floor to questions from our audience. As mentioned, we're going to try and answer as many of those as we can today. So please welcome all of our speakers as we turn things over to Dr. Lewis. Dr. Lewis?

Dr. Eldrin Lewis:

Well, thank you very much, Dr. Bevc. I appreciate this opportunity, and you see the agenda that we're going to go over. So what I would like to do is to talk a little bit about understanding long COVID. So on the next slide, you'll see that there are a lot of potential causes for long COVID. It's defined as a set of multiple conditions with diverse clinical manifestations that can affect every major organ tissue system reflecting a very potential of underlying and coexisting causes. We know that because of this, people can have a broad range of symptoms and experiences when they suffer from long COVID.

Some examples of hypothesized causes that can coexist in the same patient can be persistent virus or antigens, reactivation of other viruses, an uncontrolled immune response, as well as damage to wide range of organs and tissues including the heart, lungs, the nerves, nervous system, the GI tract, and the brain. We also know that there can be injury to blood vessels and abnormal blood clotting that can lead to comorbid conditions, and because of this, this diverse set of clinical conditions really provide the need to do a broad portfolio of therapeutic and interventions and agents that can potentially improve outcomes.

On the next slide, I would tell you a little bit about the RECOVER initiative. On the next slide, so RECOVER is a patient-centered, integrated, adaptive research network. I've been doing clinical trials for over two decades and I have to say that the participation of patients in the design, the execution of this study I think is really important, especially because we're all learning together. There is a lot to learn.

We know that the goal is to predict, treat, prevent long COVID or PASC. It's a patient-centered patient perspective, but we also know that we have platform protocols with common data elements across all of the trials. This is important so that when we look at interventions, we'll be able to compare apples to apples and that we'll be able to look at similar data elements at baseline patient characteristics to better understand and cross pollinate our understanding across multiple interventions.

This is also an adaptive approach so that we can continue to look for the emerging science and implement it into a facile way, and we know that this is a national scale. This is a broad-based problem and we want to have inclusive participation with the understanding that the impact of long COVID can be varied in different patient population scenarios and environmental situations.

So the scientific aims are to understand the range of recovery and changes in our bodies over time, to define the risk factors, the number of people getting long COVID and if there are specific different long COVID types, to study how long COVID progresses over time and how that can relate to comorbid conditions that people may have before they've developed the syndrome, and then finally, to identify possible treatments to help with the long COVID symptoms.

So how does this work? Well, there's research components and there's also information exchange, and we're glad that you're all here to hear this presentation. We know that there are patients, caregivers, community representatives, work groups, and governance committees, all who have a vested interest in the outcomes of RECOVER and are interested in being part of the solution. So we can learn from people from clinical study groups who have a lot of expert content expertise in long COVID, tissue pathology and autopsy expertise, as well as community-based study groups who are at the grassroots understanding how it impacts day-to-day lives.

We also know on the clinical science side, there's pathobiology that we need to understand and we need to use real-world data with electronic health records, mobile health apps, and digital apps, and all of this will allow us to maximize data harmonization and sharing, including understanding each study treatment with each clinical trial that we're going to run and how it relates to outcomes and how it's related to baseline characteristics.

Then finally the next slide. So this is just a snapshot of where we are and where we hope to go. So RECOVER is really going to be the largest diverse, deeply characterized clinical cohort of long COVID patients. As you know, because of how disruptive this pandemic has been, we have seen countless numbers of publications at an exponential pace for COVID, and for long COVID, we see a lot of data as well, but the pinnacle of data is really to have precise randomized trials where we can actually answer a hypothesis-driven question.

So this will provide insights onto long COVID, the prevalence risk factors, impact, and disparities from EHR, will have a robust longitudinal characterization of long COVID patients, and there are over 40 studies to characterize the pathophysiology of long COVID. Then we have these five platform protocol clinical trials. So in the future, we'll have the interim analysis, the cross-validation of EHR or electronic health record findings with clinical cohort data. We'll be able to integrate wearable sensor data in the adult cohort study, and we'll have mechanistic studies, risk stratification, and biomarker identification, which can be very helpful for individual patients as they're trying to live with long COVID. Then finally, we're launching the trials evaluating treatments. So thank you very much for your time.

Dr. Christine Bevc:

Thank you, Dr. Lewis. Next, we're bringing back Dr. Kanecia Zimmerman to share more details on the RECOVER Clinical Trials. Dr. Zimmerman.

Dr. Kanecia Zimmerman:

Thank you so much. So over the next couple of slides, I'll talk some about the general approach to clinical trials, all the people who've been involved, and talk more specifically about the platform trials themselves. I also just want to know put out there that everything ... For those of you who've been involved in RECOVER, you know RECOVER is ever changing. There's lots of things that are happening all the time as we're learning more information, and Dr. Lewis talked a little bit about that. So this is a bit of a snapshot of where we are right now, but certainly, expect things to evolve over time, and please know that there's progress that's happening as things are moving along. Next slide, please.

So there have been really so many people and groups that have been involved in this clinical trial development and the design. As Dr. Lewis mentioned and as Ms. Leverty will talk about later, patients have been really an integral part of this and patient advocates have also been really important and have had a lot of input on our working groups, et cetera, as we've moved forward with developing the trials. We've had input from clinicians, those who are taking care of patients with long COVID every single day, as well as researchers who know things about design of clinical trials, for example, and who have had prior experiences with taking care of people with postviral syndromes and even researching postviral syndromes themselves. We've, of course, had input from the FDA and other regulatory agencies as we've gone throughout this process.

It's been great also to be able to capitalize on some of the data that is coming out of the RECOVER cohorts and all the things that Dr. Lewis mentioned about all the studies that are up and moving with RECOVER to date to really identify the major symptom clusters, as well as really understand how symptoms might align, for example, with some of the tests that we might want to do in a standard clinical trial.

Patient perspectives have really informed the symptom cluster prioritization, as well as some of the interventions and other trial concepts. Then also, the broad research community has provided their input as to what things and how things should be studied. We are also happy to have some industry collaborations so that we can make sure that we continue to move these platforms forward. Next slide, please.

So there's a central goal, obviously, to identify treatment strategies for long COVID. The objectives underneath this goal are to really investigate some priority symptom clusters and their causes, to test known and novel interventions across multiple domains, so that means drugs and devices and even nonpharmacologic types of therapies and, ultimately, to evaluate the treatments to improve long COVID symptoms. Next slide, please.

So there are five protocols that are focused on symptom clusters, as Dr. Lewis mentioned, but we are really focusing not only on symptom clusters, what have we identified as really bothersome and burdensome to people, really having an impact, but also, what are the underlying etiologies and can we address those underlying etiologies? I think that's a really important dichotomy or differences between those two things, that we're really trying to address it from all different angles.

As I mentioned, there are a number of teams who've been involved with this. There have been lots of interventions that have been evaluated, but we expect that what I show you today is the start of things. We expect and hope that things will come later on, that there will be additional interventions that can be added on, and we're hopeful that the way that the Clinical Trials Data Coordinating Center and the way the trials themselves have been designed really are nimble and allow for things to happen. Next slide, please.

So one of the ways in which we are hoping to be nimble is that we've designed the trials or are in the process of designing the trials to be a platform clinical trial design. Many of you may already be familiar with how this works, but the idea is that you could potentially have a control arm, and then multiple interventions, some of which could go forward, and we could see that they're great and they might be able to ... Maybe we move them to a phase three trial or additional investigation. There are others that might not do so well or we have early indications that they're not going to do well and, therefore, could be easily be dropped and easily added to the platform itself. Next slide, please.

So other thinking around the platform protocols really is to be comprehensive and integrated. So by having things centralized at the CTDC or thinking about how we might have single IRBs and DSMBs, to make sure that there's appropriate information and appropriate expertise on the DSMB, to make sure that they're weighing in on the safety and the specific aspects of the specific protocols, but also a core group of people that might be able to be nimble and address things on a relatively frequent basis, and to be very familiar with how RECOVER is operating.

There is trial oversight, obviously, by the single IRB, the DSMB, but also the operational oversight as well and operational management of the trials. There's data analysis that are going to be centralized and then hopefully combined with some of the information that we are learning from the RECOVER cohorts, and then a large number of trial or clinical sites that might enroll in multiple different protocols so that they might actually be able to take advantage of looking at the EHR, for example, and seeing, "Oh, this person might not qualify for this study, but they might actually qualify for this study." So those centralized processes where we are really thinking very carefully about.

Then finally, long-term followup participants. I know that there have been a number of questions. For example, are there certain populations who might have brain fog that leads down the road to something like Alzheimer's? The other thing that's been really important here, and Dr. Lewis mentioned this a little bit, is to really think about how we might be able to learn as much as possible from all the trials that are moving forward. So having shared endpoints, having a very similar patient population when it makes sense or approach to inclusion in general, making sure that some of the controls might be able to be shared across within a platform protocol, but maybe even understanding how that works across protocols.

We've been very thoughtful of making sure that if there are evaluations of post-exertional malaise, for example, that are happening in one protocol, we know that just because you have autonomic dysfunction doesn't mean that you don't have post-exertional malaise, so making sure we're also looking at some of those things.

There have been lots of people who have had lots of input not only on single trials, but also across the program itself so that we can make sure that we are harmonizing information. We're using common data elements so that the information can be compared and contrasted in the future.

Then really, really important, to make sure that we are understanding mechanisms underlying not only this etiologic platform or where we're thinking about things like viral persistence or micro clots or something along those lines, but also thinking about like, "Well, if I'm in this symptom-specific platform, how can I also understand what's happening there?" So samples will be really important so that we can identify specific biomarkers and we can trend those over time and across protocols.

So the hope is that these are integrated, that these are comprehensive, and that we can achieve a lot of efficiencies to really be nimble, to be as rapid as possible once these protocols get up and moving. Next slide, please.

So as I mentioned, there are five platform protocols. On the left here, you see this idea that we are looking at these etiologic pathways, so things like viral persistence and reactivation and immune dysregulation, that might be underpinning a lot of the symptoms that we have that are manifesting in people, but also looking at specific symptom clusters, so really focusing in on those who have cognitive dysfunction, those who have autonomic dysfunction, those who might have issues with sleep, and those who might have issues with cardiopulmonary, exercise intolerance and fatigue. Next slide, please.

So I mentioned these already, but I wanted to just make sure that people understand the definitions here. So viral persistence, we're really talking and thinking about the SARS-CoV-2 virus that causes COVID-19 may stay in the body, that may be hiding out in what we're calling sanctuary sites, and it may itself cause damage. It may cause the immune system to overreact. It may cause damage to the blood vessels and clotting, and all of that might actually be playing a role in why we're seeing some of the symptoms we're seeing.

When we're talking about autonomic dysfunction, there are lots and lots of symptoms that might be caused by autonomic dysfunction or an issue of the nervous system, and it might manifest as things like dizziness or a fast heart rate, shortness of breath, problems with your digestive system where you might have nausea or vomiting, for example, or feeling really full too early and other symptoms that might be related to the autonomic nervous system.

Sleep disturbances, there are a number of things that are within this particular category, but really thinking about your changes in sleep patterns or the ability to sleep.

Cognitive dysfunction, many people know this as brain fog or the inability to think very clearly. Then when we're talking about exercise intolerance and fatigue or post-exertional malaise, we're really thinking about a person's activity or energy level that interferes with daily activities, recognizing that some of that stuff may happen or some of these symptoms might happen while people are doing activities, but some of it might happen

after people have done activities and they have what's called a crash or post-exertional malaise that we see in conditions such as MECFS. Next slide, please.

So each of these trial platforms has really been developed or is in the process of being developed by a protocol working group. They are patient representatives, they're scientific experts in the symptom areas themselves. They're experts in interventions. They are investigators who sometimes are experts in the interventions or the symptom areas, but they have submitted information to the NIH to have their intervention be in their trial thought process part of RECOVER, and then there's also representatives from the RECOVER observational cohorts.

The protocol working groups have met regularly to develop platform protocols and the appendices. That's each of the arms that we're thinking about, but also really thinking about how are we going to do that. So if we're thinking about, for example, having two drugs. So how do we make sure that we're screening people appropriately? They can go down the right pathway. Are there other conditions that need to be screened? For example, if people have issues with sleep, are we making sure that their issue with sleep isn't secondary or isn't because of something like obstructive sleep apnea? So people thinking very carefully about the details, and then even once the protocol working groups have been up and moving, we are also trying to get input from people who are going to execute this at the sites. So does this actually make sense and how would you operationalize this or are there other ways to do it better? Next slide, please.

So just in thinking about these five platform trials, and in total, we think that we will be enrolling approximately 2,600 participants for the first round of interventions. The recruitment will largely be based at sites. It will be really important for us to think about what sites have what capabilities and what populations to make sure that we're as inclusive as possible and also can get some of the scientific questions answered like specific sites have specific expertise in specific biomarkers, for example. So we want to make sure that we're capturing those people as well. We will have a range of numbers of sites for each of the trials, 25 to 100 in some cases, and then there will be more information about enrollment in the coming months. Sorry. Next slide, please.

So many of you may also be familiar with this idea of how do we get from this protocol to actually getting people into the trials. This schematic is really just to emphasize that there are multiple rounds of review not only by the DSMB and the IRB, but the FDA has done a lot of weighing in on making sure that the protocols are reasonable, that they actually might lead to something in the future, that we can answer specific questions, that they provide information that the FDA might need. So this is an iterative process that may occur for each of the protocols moving forward. Next slide, please.

So over the next couple of slides, I'll just talk some generalities about the protocols themselves. Viral persistence, in particular, it's really looking at, does the study intervention improve outcomes for people with ongoing symptoms from PASC? This will enroll approximately 900 adults who might fit into three symptom clusters, and those three symptom clusters are things like post-exertional malaise. It is things like autonomic dysfunction and brain fog. So each of those will have approximately 300 people within each of those clusters.

The first intervention is going to be an antiviral drug and we're looking primarily at patient reported outcomes but also some performance-based outcomes. So within each of these symptom clusters, performance-based outcome measures, for example, might be a neurocognitive battery. So if you have brain fog, we want to know how you're functioning and how you're telling us you're functioning, but we also want to know what happens when you take these more standardized tests. Then because we're giving a drug, really looking at safety and tolerability. There'll be up to 100 sites and our hope is that we can launch this trial in late summer of this year. Next slide, please.

So a second trial or platform is cognitive dysfunction, really looking at whether or not there are improved outcomes for people with cognitive decline that's related to post-acute sequelae of sequelae of SARS-CoV-2 or long COVID. This will enroll approximately 315 adults with cognitive dysfunction from PASC. The intervention's going to be different forms of cognitive training, and the outcomes are going to be some patient-reported outcomes, but again thinking about what people might actually be able to do on something like a neurocognitive battery. If we're taking specific tests that have been used in the PASC three different populations of people with cognitive decline, how do people perform? This will be up to 45 sites and hoping to launch in the late summer as well. Next slide, please.

A third is the sleep disturbances, and looking at whether or not a study intervention improves

patient-reported outcomes for people with sleep disturbances from PASC. There are a number of different types of sleep disturbances. So there's hypersomnia, for example, but there's also things that are like circadian rhythm disorders or insomnia. So we will be looking at these phenotypes separately for now and enrolling approximately 474 adults with sleep disturbances, predominantly hypersomnia, from PASC. Also looking at things like patient-reported outcomes, sleep outcomes. We want to make sure or we want to understand how long people are sleeping, when they're going to sleep, et cetera.

There will be some pharmacologic and nonpharmacologic therapies that will be here. So for the pharmacologic therapies in particular, interested in safety and tolerability. So we performed in up to 100 sites and anticipated launch in the fall. Next slide, please.

For exercise intolerance and fatigue, we're really interested in whether or not a study intervention improves outcomes for people with exercise intolerance symptoms from PASC. We'll be looking at approximately 360 adults, and the intervention here is cardiopulmonary rehabilitation. There are both patient-reported outcomes and functional outcomes as well. This will be done in up to 50 sites and launching hopefully in the fall of this year. Next slide, please.

Then finally, autonomic dysfunction, so thinking about whether or not the intervention helps improve outcomes for people with autonomic symptoms from PASC. We're looking at 360 adults who experience these specific symptoms, and we are looking at not only pharmacologic therapies, including immunotherapies, as well as nonpharmacologic therapies. We are interested in not only patient-reported outcomes, but also, there are obviously lots and lots of tests and evaluations that can be done for autonomic dysfunction, specifically because of how many systems or organ systems this really could affect, so also looking at some of that, and interested in safety and tolerability. This will be performed at up to 75 sites and launched later this year. Next slide, please.

All right. With that, I will pass it over to Ms. Leverty.

Dr. Christine Bevc:

All right. Thank you, Dr. Zimmerman. So we're going to bring on Ms. Renee Leverty to give us some information about the patient and community engagement in RECOVER Clinical Trials. As a quick reminder, if you have a question for any of our panelists, you can drop those into the Q&A feature and we will try to get to as many of those as possible. All right. Renee?

Ms. Renee Leverty:

Yes. Thank you. Hi, everyone. So I am the Associate Director of Research Together at Duke Clinical Research Institute. What my team and I strive for is to develop infrastructure and systems to amplify and bridge lived experience knowledge so it can influence and impact study design and study conduct. Next slide.

So for patient engagement in the clinical trials, patient representatives are on the PASC intervention prioritization committee and suggest therapies and interventions that they either have personal experience with or have seen work within the long COVID community. Patient reps have completed surveys and questionnaires and were involved in the ROA review process, and patients are integrated into protocol working groups. Next slide.

So engagement in the platform protocol, RECOVER patient representatives that were part of the review of applications for clinical trials were invited as experts to be part of protocol writing teams. Two patient and community reps are on each protocol working group. Being a member of that working group, they attend working group meetings, receive the protocol and DSMB feedback in various stages, the informed consent, and are part of email discussions and exchange of ideas.

There's an extended group of patient reps, what we call the small group, which are associated with the protocols but not directly on protocol working groups. This group has met with the study co-chairs and co-investigators outside of the larger working group meetings. The goal of that is to create an opportunity for more focused conversations on patient priorities.

Additionally, three out of the five small groups, again, one linked to each platform protocol writing group, have met with NIH leadership and the other two meetings are being planned. Patient representatives are also members of the Clinical Trial Steering Committee, and since patient engagement may be new to individuals on the protocol working groups, we created engagement training for the operations team and support for the researchers.

We brought together diverse patient and community reps who are newer or have never been in

research to assess protocol visit cadence and activities to better understand the patient journey and the potential burden, and also engaged with the National Community Engagement Group, the NCEG, which serves as a central forum for RECOVER to promote meaningful discussion through partnership and shared decision making. Next slide.

So impact of patient experience on clinical trials, helping align unmet needs of patient and communities with the research goals, develop endpoints and outcomes most meaningful to patients. There have been robust discussions around inclusion, exclusion, benefit, and risk. Create least burdensome procedures and schedules, as well as sharing experiences and recommendations about what data to collect, work to decrease barriers to recruitment and participation, increase understanding around cultural beliefs and values in order to ultimately create an inclusive and supportive research participant experience.

This will happen later in the program, but develop strategies for engagement and distribution of findings. We understand that dissemination of findings needs to be done in partnership with patients, communities, and advocacy groups. Next slide, please.

So we want to thank the patient and community representatives who are on the protocol teams and small groups who are attending meetings, reading incredibly dense documents, and giving feedback while experiencing a complex and at times debilitating chronic illness, the RECOVER National Community Engagement Group and subcommittees for their leadership and insights. To patient advocacy organizations and people living with long COVID, we know this work to understand path started long before we came to the table, and we are thankful for your work and how it informs clinical trials. Next slide, please.

You can go to the next slide. Thanks. So future updates about clinical trials in all aspects of RECOVER research can be found by visiting recovercovid.org. We will post the final clinical trial protocols when they are ready and also provide updates about enrollment status and next steps. Thank you.

Dr. Christine Bevc:

Thanks, Renee. I want to bring in two of our patient reps that have been part of this process. So let's go ahead and bring in Christine Maughan and Marta Cerda to help us better understand what these clinical trials mean from the patient perspective and what questions they have about this, about these clinical trials. So Marta, do you want to start us off? Then we could bring in Christine to share her thoughts as well.

Marta Cerda:

Thank you, Christine. I'm Marta Cerda. I experienced RECOVER in a couple of ways. First, I was a RECOVER study participant. There, I answered questions and have annual examinations, which helped me to understand that I've lost 30% of my taste and smell due to long COVID, for example. Then secondly, I experienced RECOVER as a participant in the steering committee. As has just been mentioned, we do participate as patients in community engagement committee and in discussions around the development of the clinical trials.

I also wanted to add that my agency also helps with community outreach for the RECOVER study itself by working to engage minority members in addressing their fears and concerns and digital literacy issues so they can enter the study themselves to learn more about long COVID.

Most important for me, participating in the RECOVER taskforce at first was nerve-wracking a little bit because I was not sure I was going to be able to keep up with these complex discussions around this very complex illness, but fortunately, due the fact that they do take time to explain very carefully their decisions and the protocol, I was able to provide input on how this illness has impacted me and on the clinical trials as they have been developing.

What has happened as a result is that I have developed a higher level or a deeper understanding of my own long COVID illness. For example, through participating in a breakout group on the trials around the stomach, that is where I learned that vomiting and nausea and stomach pains, random stomach pains that I had been experiencing a few months ago are a part of long COVID.

Next, we had meetings around PEM, exercise intolerance, and it was during these discussions of this mild, moderate, and severe PEM that I realized that I myself had PEM. I thought I was just not wanting to exercise, but in listening to those discussions around the development of this trial, that's where I had an understanding that I too have those two illnesses. This was very important to me because I had been to my primary care physician and that physician had no answers or no answers to me around what these issues were or what could be done about them. So for me, my participation in the taskforce has been invaluable.

Next, I did want to say that the community engagement team really thoughtfully works on

dealing with bringing in the Latino, African American, and Asian communities. I participated in the development of the marketing materials for those communities, for example, so we can better draw in communities that are deeply impacted by long COVID, so we can find treatments and hopefully a cure at some point for this illness.

Next, I did want to say that I do have many, many hopes for the trials. I am hopeful that there will be some form of treatment or whether it be medication or the therapies that can assist with issues that I do tackle every day with brain fog, as was mentioned earlier, with heart racing, issues around my lungs, and sometimes stuttering, for example. Some of, I would say, the more severe aspects of long COVID, I am very much more hopeful through my participation in the taskforce that we will come up with solutions going forward.

Lastly, I wanted to say that when I first entered, the taskforce I was concerned about whether or not I would be able to participate because there are very challenging conversations between scientists and physicians, but I have to say the team carefully explains what is going on and they gave us as patients opportunities to provide input. That is why I have been able to contribute to the trials so they can better address the issues that we face as patients tackling this, again, complex illness every day. I'll turn it over to Christine Maughan.

Christine Maughan:

Hello, everyone, and thank you for joining us today. As previously mentioned, I am one of the patient representatives on the steering committee for clinical trials and was asked to share a bit about my experience with RECOVER so far and my hopes for this work moving forward. My involvement with RECOVER started due to an early COVID infection and a community of patient advocates who pushed for answers at a time when we had none.

In March of 2020, I began experiencing my first COVID symptoms and I later tested positive in early April. At that time, we had been told that if we caught COVID and we're lucky enough to survive, we would be better in two weeks. When those two weeks came and went and we were still sick, we knew something was very wrong.

In those early days of the pandemic when we did reach out for help, many of us were met with confusion at best and disbelief at worst. So we turned to each other. Through various online forums and social media outlets, patients who were still sick long past those 14 days began posting their symptoms and began forming groups and began advocating for recognition, research, and care. During this process, we learned that it was not all in our heads, that we weren't alone, and that this was so much more common than any of us could have imagined.

When I first joined the Utah COVID-19 Long Haulers Facebook group, a group I now help moderate, I was the third member. We now have almost 4,400 members. It is through this community and its fearless leader Lisa O'Brien, who I know is listening in today, that we began discussions with researchers and staff at the University of Utah advocating for one of Utah's first long COVID clinics and eventually found our way to RECOVER.

Now over three years later, long COVID symptoms still impact my daily life, and while my good days are better than they used to be, I still have many bad days when I struggle to even get out of bed. Due to these ongoing symptoms, I now participate in the RECOVER observational cohort as a long COVID patient, where I've been asked to contribute everything from blood samples to six-minute walk test and so much more.

Many of us, myself included, have helped shape RECOVER due to work as patient, community, and caregiver representatives. I serve on the National Community Engagement Group or NCEG, a group tasked with ensuring that RECOVER research meets the needs of patients, caregivers, and community members. I am also on the publication subcommittee, a group which helps ensure patient community reps are included and engaged in the publications process of RECOVER. I serve on the steering committee for clinical trials, the focus of our presentation today, and the protocol working group examining the possibility of viral persistence and potential treatments therein.

I attend these meetings for my couch with my feet elevated on a stool to help counter my orthostatic intolerance, something I know many of the patients listening today can relate to, and I often leave my camera off to help conserve my energy. Through all of this, I take with me those early discussions and sense of community we formed as patients when we had no one to turn to but each other. I know I may not always get it right and I've had plenty of stumbles along the way, but I try to remember every story that's been shared with me the past three years and ask myself, "How best can we serve those patients?"

My hope is that RECOVER will learn from the work of these patient advocates and understand that we are the experts of our own lived experiences. In order to know how best to treat long COVID, we must first understand its impacts, and who better to learn that from than those who live with it daily?

Thanks in large part to the tireless work of patient advocates, we have reached a place where groups such as RECOVER are beginning to trial treatments. It is also my hope that throughout this process we continue to engage with those who live daily with the struggles of long COVID and that we may find meaningful ways to improve their lives. I'm grateful for this opportunity, but more importantly, I am grateful to the many patient advocates whom I know are listening in today. We would not be here without you. Thank you.

Dr. Christine Bevc:

Thank you, Christine. I want to invite our entire panel to turn their cameras back on and join us. We have a good amount of time for some questions. So I want to pose our first question to our patient reps while we have them to ask them, what have you learned about the clinical trial development process through this experience? What continues to motivate you there?

Christine Maughan:

I can take this, and thank you. I think what has struck me the most is just how much work goes into these clinical trials. It's been really interesting to hear all of the different experts give their advice and opinions and to see the way that the trial's been modified along the way. I've definitely learned a lot. It's been an interesting process.

Marta Cerda:

Yeah, I would have to agree that seeing the debate between the researchers has been fascinating. So someone will come in with expertise in that particular area and they'll bring that information to the team and that will alter the way the trial proceeds and the protocol is developed, so seeing that engagement, and I have to say the commitment of this taskforce team is incredible. They're really committed to finding solutions, and so they do listen thoughtfully to each other and to their colleagues. So that process has been a good one to learn about. Before this process, I had only seen presentations about clinical trials, so I understood the framework, but seeing the actual going from point A to point B has been a good learning process and they have accepted our input always.

Dr. Christine Bevc:

All right. Thank you. I just wanted to quickly introduce the additional member to our audience, Dr. Adrian Hernandez, the Executive Director of the Duke Clinical Research Institute at Duke University. Welcome. Our next question, and this also is going to hit on a couple of the questions that we've seen come in from our audience members about recruitment. So how are these clinical trials recruiting participants? How are you going to reach underserved communities and those who may not know that their symptoms could be long COVID?

Dr. Kanecia Zimmerman:

I'm happy to start and happy to have people add when it's appropriate. So the recruitment will primarily be site-based. The idea is that we would have a wide range of sites over a wide range of geographic locations and making sure that the sites have certain capabilities. So there may be sites that we're looking for that, as I mentioned, have expertise in something called PBMCs, which is special labs that could be done, but only certain sites could actually do them because they had the appropriate things to process, et cetera. So we would be looking for sites that have that type of expertise.

There are also some sites that might have the capabilities of doing things like cardiopulmonary exercise testing. Not every site can do that, but we want to make sure that if that trial calls for at least some sites to have cardiopulmonary exercise testing, for example, we want to make sure that we're including some sites that have that capability, but we also are really, really interested in being inclusive as far as our population, so looking for sites who care for patients who may be underserved, who usually aren't able to participate in clinical trials. As we've been designing the trials, we've really tried to be very thoughtful about what is the lowest common denominator of the sites. What is it that we actually need from every single site to make sure that sites that don't necessarily do clinical trials on a regular basis, although they have the want, the desire, the population, how can we make sure that they're also included?

I think as far as the second question, Christine, just thinking about how do we make sure that

people who don't know that they have long COVID can understand that, that's our job. That's our job of everyone that's part of this panel. It's the job of hopefully all the patients and patient advocates that are watching today. We got to get the word out because it's very possible that people like Marta, for example, Ms. Cerda, she mentioned that she didn't even know that that was one of her symptoms, and there's certainly other populations. We've done listening sessions that say like, "Oh, my gosh, I just thought I was really, really tired because I had to work so much because the economy isn't that great. I'm working two jobs now as opposed to one, and I just thought I was really, really tired." So those types of things, it's our responsibility to get that information out.

Dr. Adrian Hernandez:

One other note along with what Kanecia said is that I think everyone's hoping that the RECOVER program is a continuous process. So as results are generated from their clinical trials and if they have an impact on an area, how can we get that to every corner of the US and around the world as soon as possible? It seems like this community that's extremely motivated because either they've been in touch with the people who've had problems with long COVID or living with it and so forth are going to be the greatest channels for getting results to the people who are suffering from long COVID. To Kanecia's point here, it's making sure that people are recognizing this. They may assume that they have something else and aren't actually seeking attention. So this seems like it's going to be a full on affair.

Marta Cerda:

I was just going to add that I'm very passionate ... Sorry. I'm very passionate about letting people know the symptoms that I do have on panel discussions, I'm doing another one next week at the state of Illinois building downstate, so that they understand that they're not alone, that other people have these issues around brain fog or stuttering or shortness of breath, all of that. So I have engaged even being interviewed here by ABC 7 Chicago. So I get out the word about those symptoms. I do think far too many people don't know they have long COVID and they could get help. Sorry, Renee.

Ms. Renee Leverty:

I'll add that we have bilingual staff and also look for sites with bilingual staff developing community engagement toolkits. We want to partner with already trusted resources within the communities at a local and national level. So please reach out because we know it's these already formed relationships that will help us share the messaging about the work of RECOVER.

Dr. Christine Bevc:

For those that are interested in reaching out, how do they do that? Where can they go?

Ms. Renee Leverty:

Yeah, we can put the email in the Q&A.

Dr. Christine Bevc:

All right. Great. Then Dr. Zimmerman, on the site selection, are those forthcoming? I know you've mentioned a couple months from now. When could folks expect to hear about those and find out where they are and whether they're near, there's a site near them, and what they should do if there isn't a site near them?

Dr. Kanecia Zimmerman:

It's a great question. So yes, that information is certainly forthcoming. We have started getting some interest from sites or at least sending out information like, "Do you have this? Do you have this capability? Do you have this capability?" to see whether or not sites are interested and who might be interested and making sure that they can identify who the people are at their team, sorry, who their team is actually at the site to be able to do some of the work. So that process is happening right now for the trials that may start up earlier rather than later. The information about the sites will eventually be posted on a recovercovid.org. Is that right, recovercovid.org? So that will be there.

Then I think that we need to be, I think, very thoughtful about where ... If people do not have a specific site that's in their vicinity, there is a list right now that's being generated for people who are interested in clinical trials to make sure that they can have the appropriate information. Yeah, I hope that's helpful, Christine.

Dr. Christine Bevc:

Yeah, and again, all this is we're recording this, so it will be posted and then also the questions

and answers are going to be compiled into a document as well and posted on a website for folks. So the next one, I want to get into the effects of cardiopulmonary rehabilitation and PEM, and the post-exertional malaise, and this is a question I am seeing come in over here on this side. There are lots of questions about this, and I wonder if you guys can help unpack that a little bit and how that's fitting into the exercise intolerance protocol and how you're going to monitor for safety and the different decisions that went into the measures and that component. So Dr. Lewis, Dr. Zimmerman, do you want to start us off and then we can open it up or who wants to go first?

Dr. Eldrin Lewis:

Kanecia, do you want to start?

Dr. Kanecia Zimmerman:

Sure. I can certainly start. So I will just start by saying that this is a work in progress to really define not only the intervention like what exactly that looks like, but who the appropriate population is for this particular trial. I want to say also that we have certainly heard the patient feedback. Here, there have been lots of people who've given feedback, but also the people in the working group, the patients in the working group have been intimately involved in this process to tell us, "Absolutely not. That's not appropriate," or "This seems to be appropriate," and that's gone back and forth with executive committees and steering committees, et cetera.

So people are committed to getting this right and to making sure that it is first and foremost safe. So while I can't tell you exactly what the cardiopulmonary rehab intervention looks like right now, I can tell you that safety is at the center of everything that's being done from the inclusion criteria to the intervention itself. We are very much aware of those with post-exertional malaise, those with MECFS phenotype, and those also who have exercise intolerance where they're having difficulty as the activity is happening. We want to make sure that we are thoughtful about all those things.

We also want to make sure that once we have the trial, once there's the appropriate population that's in that trial, that we in the future are also communicating what happens, and we're communicating it with all the nuances so that it doesn't necessarily turn into a global recommendation for everyone if that isn't the population who is in the trial. So hopefully, that's a start. Dr. Lewis, please take it away from there, but I just want to emphasize there's the DSMB. Our teams are being very thoughtful about it. Safety is number one on the list.

Dr. Eldrin Lewis:

Absolutely. It's really challenging, and certainly, we've heard a lot of the feedback. I want to say that the PASC population with exercise intolerance is different from, in many ways from your classic PEM, especially the severe PEM, but that being said, because they're overlapping symptoms, what we don't want would be to have people who have severe PEM as an initial component of this trial.

One of the things that I would just emphasize is many times when there has been a decade or two decades of clinical treatment, perception of understanding, it becomes really challenging to answer a question because we feel that we know the answer. I used to give lectures on this in cardiovascular disease as a heart failure and transplant cardiologist. Adrian would know this as well. For a long time, we never gave beta blockers because we said, "Why would you give a beta blocker to someone who is chronotropically or inotropically challenged?" So we basically didn't use a therapy for a long time in heart failure because of the perception that beta blockers will harm patients.

In fact, I still remember when I was early in my career when someone actually screamed, "Why are you trying to kill my patient by giving beta blockers?" when the first trial came out that basically showed that beta blockers were associated with 34% improvement in survival. One that a lot of people know is hormone replacement therapy. When I was in medical school, we used to use HRT as a standard treatment for women who were perimenopausal, thinking that we were improving cardiovascular risk until we did the WHI, and when that was done, and it was a randomized trial, you saw that there was actually no benefit and in fact harm. So once again, one of the hardest things to do is to actually test it.

What you want to do is to ensure that each participant, each 360 of those participants will be studied in a safe way. I think it's really important that we understand this. The last example I will give, and then I'll pass it over to Adrian, is exercise. If you look at guidelines in years past in heart failure, they would say, "Why are you going to exercise? That's dangerous. People with heart failure cannot exercise. They're going to have arrhythmias. They're going to drop dead. We should not recommend exercise. People with heart failure should sit in their chair until they die."

That sounds cruel, but that's basically what we were doing, and we didn't realize until we

actually, in a safe way, study can exercise make a difference. That actually starts saying, "Okay. You know what? You should exercise. Here's a safe way to exercise." You're not going to start with the sickest people when you're going to do that protocol, people who are on life-sustaining intravenous drugs. You're going to start with the healthier population with heart failure and then do it.

There was a cardiac rehab study where you looked in heart failure patients who were moderate to high risk and randomized them to rehab versus usual care, and randomized over 800 patients in 81 centers. So it can be done, but the big thing is to make sure that it's done in a safe way and then answer the question once and for all with the randomized study. Adrian?

Dr. Adrian Hernandez:

Yeah, no, I'll just note that I think this has to be one of the hardest areas in health and science that at least I've ever encountered. I think for anyone who's lived unfortunately with long COVID or PASC, I mean, they're going along with their life and not expecting something like this, and especially early on when COVID comes out, like I said, like, "Oh, it's a bad flu." Well, that's the really bad flu. What are we talking about here? So I think if you just think about the population and essentially a new disease that has some overlap with other syndromes or other areas, it's still really challenging because you don't fully understand all the different causes and contributing factors here, which also makes it hard to understand what's the different types of interventions.

Then when there's similarities with other areas of health which have been studied and have some real challenges of understanding what works, then you start having other difficulties in saying, "Should we just assume something on this way that it won't work or it will work or this and that?" That is defined as research, unfortunately, that we don't know all the answers.

What we have here is a platform to get those answers, and it's going to be a continuous journey. Eldrin highlighted some examples in different areas of health for which for many years we had assumed something so-called dogma, and it turned out when you did the larger study, the dogma was not quite right. Actually, it was the opposite answers here.

So just from the Q&A and the conversation that's in the dialogue here, it's very clear that there are no easy answers here. Everyone's committed to get the best answers in a better way than we've had. I think this is going to be a continuous process with the platform for RECOVER.

Also, I want to thank everyone for reaching out and being really strong advocates in terms of importance of PASC and long COVID. Everyone's listening. Final thing is that I wish we had consensus on everything. I think the difficulty in PASC and long COVID is that there is not 100% consensus for most everything. I think in some cases we get to 51% and say that's consensus, but it's not a consensus for every component, and it's certainly not close to 100%. So I think that underscore is why it's so important the efforts that we have here.

Dr. Christine Bevc:

So just to quickly add on to that, are there separate analyses that are planned for patients that are experiencing PEM versus those without PEM in the protocol?

Dr. Kanecia Zimmerman:

So the details, Christine, are still being worked out, I will say. As I mentioned, there are thoughts about which populations should necessarily go into the trial, for example, but understanding that PEM is a condition that lots of people can experience and lots of people, particularly with long COVID, can experience. Certainly, we want to make sure that after any of the exercise sessions, that there's followup to evaluate everyone for whether or not they have symptoms of post-exertional malaise, and to be able to then alter whatever your exercise intervention is in order to make sure that people stay safe during that. So yeah, it would be a blanket safety evaluation for every person in the trial because we know that everyone might be at risk for a developing PEM.

Dr. Adrian Hernandez:

Then I guess the other thing because I saw some of the comments that come through is that, and it's very clear the concerns about people who have PEM or have had PEM or have seen people with PEM and the different issues with exercise intolerance that's also been seen with long COVID. So I think one of the things that's come up through the various discussions is being really attentive to the safety and safeguards and how things should be monitored or even included as part of the intervention. So I think these are examples where people are trying to translate what's been the prior research scenario, but also noting that we may or may not

know fully what the exact overlap is with long COVID, PASC, and MECFS. So it's complicated to say the least and those living with it know that fully.

Dr. Christine Bevc:

All right. We may circle back to this topic, but I want to make sure we can cover some of the other questions that we've had. One of these is that there's good evidence that biochemical signals of inflammation in individuals with long COVID are not the same in blood and in cerebrospinal fluid. Success of any trial is going to involve documenting improvements in biomarkers such as these. So have any biomarkers been developed that can reliably be utilized or the discussions around those?

Dr. Kanecia Zimmerman:

I'm happy to start again. Let's see. So we are still learning. We're still learning, right? There's so much that we have to learn about PASC. There's so much that we are hoping to learn from RECOVER along cohorts. There's lots of biomarkers and things that are being studied within that space, and then people outside of RECOVER, lots of things that are being studied and people are trying to keep up with the literature. I think every week we get some email about a new thing that has come out with regard to papers that we should be reading and evaluating.

I think first and foremost, we are very interested in making sure that the success of the trials is defined by patient improvement, so that's how are people feeling and functioning, but you're right in that biomarkers are also going to be an important part of this. Some of those, if we're thinking about inflammation, if we're thinking about viral persistence, some of those things we might be able to use from prior disease processes, for example, or if we're thinking about reactivation being something, can we measure EBV at the beginning and then at the end? So some of the things are going to be in existence from what we already know and we will learn whether or not they're improved or not as we go through the course of the trials.

There are some more specific things that people are looking at, specifically to measure viral persistence, for example. There's an assay that has shown some differences in the spike protein antigen between those people who have PASC and those people who don't have definitions of PASC, and we're hoping to incorporate some of those things within the trials themselves, but lots of things still to learn, lots of opportunities out there. Interested in people's thoughts and ideas, and also want to make sure that those biomarkers are aligning with how people are feeling and functioning.

Dr. Adrian Hernandez:

One of the things to note is that through the whole RECOVER program, including the clinical trials, because there's these tensions of so many unknowns like trying to understand exactly what's happening or causing long COVID with the tension of like, "Hey, we need answers now. We need interventions so we'll improve someone's health, their function, their quality of life," how to do things in parallel? So having all this available to develop some of those answers is really critical because I don't think anyone in this community is really excited about serial answers that takes decades. So that's why there's so much trying to be done to do things in parallel with a multi-pronged strategy with different platforms for different areas of long COVID.

Dr. Christine Bevc:

I want to make sure we're also getting our patient voice in this. So Marta, Christine, are there any items that come to mind that you want to address or that have prompted thoughts from this discussion so far?

Marta Cerda:

I can say that during the process, I did give my input and the fact that although it may be difficult for me to do an exercise intolerance exam, our exercises for them that I would do so because of my deep desire to have a treatment or a remedy. So as long COVID patients, I would say the majority of us are willing to go back and forth for testing so that we can get closer to a treatment or a cure. There's a willingness there that perhaps I would not have in other cases, but there is, again, heightened sense of wanting to resolve some issues around being able to exercise a little bit more would be helpful to me.

Also, I had to say most important would be some of the brain issues that we have challenges with memory, fog, memory loss, stuttering. I never stuttered in my life and I forgot to mention the other important one is anxiety. I never had an anxiety attack in my entire life, and all of a sudden I've had a couple of those. They're very disconcerting and I would like to find some form of treatment. So there was a willingness from the majority of the patient population to undergo testing and trials in order to get closer to some form of treatment.

Dr. Christine Bevc:

I think that also echos one of the other questions that we received about how the trials are going to be pairing the symptom clusters and enrollment into the different trials. Are patients within a trial then subgroup by a symptom cluster, and then what if they have more than one symptom, are they then restricted or limited or who goes where? How can that help be decided?

Dr. Kanecia Zimmerman:

I'll talk about viral persistence as an example. So we know certainly that up to 60% of patients who have long COVID have overlapping symptoms. Some of that data has come out from the RECOVER long COVID cohorts and other health sources, but we have tried to be fairly deliberate about allowing people within the viral persistence protocol if they are the first arm, for example, if they have not only brain fog but also autonomic dysfunction or also PEM, that they might potentially be an option to enroll for all of those three symptom clusters.

There are certain inclusion criteria for each of those symptom clusters. So there's not only saying, "I have brain fog," but there's also other information and other tests that need to be passed, I guess, in order to be included in that particular trial, but we would be very interested in the worst symptoms if you didn't pass the other ones, that that would be the worst symptoms, that brain fog might be your worst symptom, but you might not have as much issue with the other two symptoms. So within viral persistence, there's the opportunity to be across.

We have tried to be pretty thoughtful about making sure that people aren't necessarily in multiple trials themselves at the same time if there's drugs involved, for example, because we want to be able to understand the effect and we don't want one thing affecting another, but the details about how that will all work to make sure we're as inclusive as possible, allow people to be as part of however much they want to be as possible, the details of that are still being worked out.

Dr. Christine Bevc:

All right. I want to circle back to Christine again to share her thoughts on this discussion. Christine, what's coming to mind for you?

Christine Maughan:

Sure. I think what came to mind the most was just that I appreciate that we're having this discussion and that we're having it in this space. It's a really good opportunity to get input from patient perspective and for those questions to be answered. I'm looking through the Q&A and I see some names I recognize, some that I don't, and I just want to assure everyone that we are listening.

Dr. Christine Bevc:

Yeah. We've got a lot of questions down in there, so we're going to try and get through a few more of these before our time is up. This goes back to our patient reps about just, can you expand a little bit more about how patient input was incorporated into the planning? Is it weighted? There's been concerns about patient input not being given and just really valuing the input of those who have lived the experience. So Christine, Marta, I think this might go to you and then a little bit to Kanecia, oh, and Renee.

Marta Cerda:

I can give you an example, actually. I was in, again, the gastrointestinal breakout group and speaking about what was really most important to me. I did give a comment that while it's disturbing to have vomiting and nausea and I'm experiencing that right now, actually, some nausea, it's not as important to me. I weighed it. It's not as important to me as my heart racing or my lung's not functioning well. I have scarred lungs, for example, right now. So I was able to give that discussion because it seemed that there were going to be some challenging clinical trials with that group.

So, they did take my feedback and they said, "We hear you. We're putting this in our notes," and they include this in our discussion. So it was the weighing of the importance of that study was taken into account. I felt it was, and it was told to me that they were moving it forward. So that's just one example. Renee?

Ms. Renee Leverty:

Thank you, Marta. So the patient and community reps on the protocol working training teams are full members. So as researchers come to the table with past experience learned and lived of how they see clinical trial being developed or areas to focus on, the same works with the patient representative. It's not a voting

structure, it's a consensus structure. It's developing knowledge, co-developing knowledge, and sharing knowledge and trying to lift and create a protocol that is taking in all those factors.

Now, one thing that we do is we do document patient and community feedback and we follow up regarding influence. We want to do that because it helps make this protocol better to know that if something was recommended as part of a team and it wasn't accepted, that we, I'll put myself in the researcher camp, we as researchers know why. It helps researchers think more critically about decisions they're making and it's a conversation and it's consensus.

So we're lifting systems to have the patient input as part of the working group team to be equal because we're developing strategies for things to be created, the protocols created through consensus, but again, not like researchers, not every item that a patient rep may recommend may not be in the protocol, and it's the same for the research team on the protocol. It's built together.

Dr. Adrian Hernandez:

Hey, Christine, one other note just to add to that is it's not going to be done there just with the protocol, it's going to be through and through. So as the studies are launched, there'll be some early learnings in terms of what the experience is and/or getting others to join and then finally the results, so how that's disseminated and shared with the communities. So my guess is that just like the beginning of this efforts has been complicated, getting results out in a way that's understood will also be complicated. So making sure people understand that and especially with all these overlapping issues of the different symptoms and syndromes.

Dr. Christine Bevc:

Thank you. So the next question, and we've seen this come up again also, few questions in the Q&A and a that we've received. How's real world data such as electronic health records being integrated into these trials? How are you factoring in patients who couldn't get those PCR tests earlier in the pandemic or those who have had vaccines and been boosted or not been boosted? How is all this playing into these trials?

Dr. Kanecia Zimmerman:

Christine, I will start with the people who couldn't get information or couldn't get tested at the time. I will say that this is an area where patient advocacy, especially, Christine, on this call around has been so awesome in making sure that I not only am aware of it, but also really thinking carefully about this and thinking about this across all the protocols in RECOVER. We are opening up the RECOVER trials to make sure that some people who have probable or suspected COVID could in fact still participate, especially if they had probable or suspected COVID prior to when tests were widely available so that we can make sure that we are understanding that population as well.

It's not just we understand that some of those patients have the most severe disease, we also understand that those patients didn't necessarily have access to testing because it wasn't widely available, but there's also a lot to learn from that particular group. So our hope is to understand how duration of symptoms might even affect how you may respond or recover in these particular trials. So certainly, thankful for Christine and Marta for helping us to really be thoughtful and inclusive of patients who didn't have access to testing. I forget your other questions, Christine. I'm really sorry.

Dr. Christine Bevc:

Yeah. It was just how this fits into the larger RECOVER picture. Clinical trials are one piece and then there's the real world data component and the observational cohort, and how is this all hitting, fixing, coming together to identify some of these solutions?

Dr. Kanecia Zimmerman:

Other people can probably weigh in on that as well, but we have meetings with the RECOVER cohort leadership, the adult cohort leadership in particular, and making sure that we're asking very similar questions so that we can cross compare information using things like the common data elements that have been identified. There will be both RECOVER sites and non-RECOVER sites within the clinical trials, but certainly, those RECOVER sites will allow us to capitalize on some of the information that's already been gathered within the RECOVER data.

We're going to use the EHR to try to identify what we call phenotype patients so that we can

more quickly identify them for the trial. Then I'm excited about the wearables that the cohorts are using as well, and that's a form of real world data to be able to really track heart rate and things of that nature on a consistent basis that we are also collaborating. Actually, after this, I'm going to a meeting with the RECOVER cohort to figure out how we might be able to do that together.

Dr. Christine Bevc:

All right. Thank you, Dr. Zimmerman. So we have time for maybe one, maybe two more questions here. Renee, did you have a question that you had seen pop through that you wanted to make sure that we were able to touch on?

Ms. Renee Leverty:

Well, I was going to actually type a response, but I accidentally hit answer live, but somebody wrote about patients as researchers, and you're right. So if my language created a separation of somebody fits in a certain box in another box, I'm wrong on that. So I want to acknowledge that, and that's what I was going to type to you, but I'll answer it live instead.

Dr. Christine Bevc:

Thanks, Renee. All right. Just to help us close out, what are you looking forward to most in the next few months? What can our audience be excited about, be looking forward to? What are you looking forward to? Everybody's on deck for this one. So next few months, what are you looking forward to? What should our audience know?

Dr. Eldrin Lewis:

I'll start. First patient, first visit. Nothing more exciting, and I talk a lot and I apologize for my laryngitis, I'll just emphasize that when I'm in the CCU, I teach that the worst thing to do is nothing. So let's answer a question and then if the answer moves the needle, great. If it doesn't, we've learned and then let's move to the next intervention.

Christine Maughan:

Yeah. I would echo what Dr. Lewis said. I am just really looking forward to the clinical trials launching and to see what the results are.

Dr. Adrian Hernandez:

So I'll add to this, and so it's not only just getting the different trials started, but also having these different platforms going. So to get to Eldrin's comment, it's being able to more seamlessly answer more and more questions about long COVID. I think just a discussion today, I saw all sorts of things like we have over the last year ideas and concepts that need to be tested. So how do we move those things in a streamlined way? The hardest thing for everything is building that foundation to do so, and especially if you think about the five programs here, it's really setting up the foundation to continuously do those studies to give people answers, but certainly, the first patient enrolled, first participant enrolled for each of these programs will be terrific, and then also the first results that come out.

Dr. Christine Bevc:

All right. The clock is against us. Couple seconds, Renee. Go.

Ms. Renee Leverty:

I'm excited to continue to work with patient and patient advocacy groups to bridge that lived experience and for the first clinical trial to stand up.

Dr. Christine Bevc:

All right. Marta.

Marta Cerda:

I had COVID. I got COVID in November, 2020. This has been a long haul, so I'm very optimistic that these clinical trials will create some form of treatment that will alleviate some of my issues. So I'm very excited.

Dr. Christine Bevc:

Great. Dr. Zimmerman, close us out.

Dr. Kanecia Zimmerman:

Getting started, moving. Let's go.

Dr. Christine Bevc:

All right. Please join me again in thanking our patient representatives and the folks from our clinical trials team here today for taking the time to share these updates with us. Thank you to our audience too for all of your great questions. We had so many and we weren't able to really get to all of them. We could spend days, and that's what this team has actually been doing is spending months working on these.

The FAQ to those questions is going to be posted along with the recording of this webinar and links to those previous ones on the November webinar on biomarkers. Those will be available on recovercovid.org. That FAQ is going to include answers to the questions that were submitted that are relevant to today's webinar, including those that were submitted in advance or during the session. So if you didn't see your answer or didn't hear that answer, look for that FAQ for those responses. Anything that's more general or broader can be addressed in future webinars, as well as some of the broader questions in our general FAQ section as well.

So as we close, we just want to invite you to come back and attend our future R3 webinars. We're going to continue to dive deeper into some of these topics that have been discussed. If you haven't already, sign up to get the updates for future announcements. We'll be back on May 9th for our next webinar as we continue to look at RECOVER in Action, and we're going to be diving into PASC in children and adolescents. So if there are topics that you want to learn more about, be sure to drop those into the survey on your screen. That chain is going to be flashing up momentarily, and just thank you again for joining us and being with us, and we look forward to seeing you again in the future. This concludes today's R3 webinar. Thank you.