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CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

Virtual Public Meeting on Patient-Focused Drug Development for Long COVID

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C O N T E N T S

C O N T E N T S

PROCEEDINGS

WELCOME

MS. BENT: Good morning. Thank you all for joining us today for our patient-focused drug development meeting for long COVID. I'm Robyn Bent, the director of patient-focused drug development within the Center for Drug Evaluation and Research at the FDA. I will serve as a discussion facilitator for today's meeting.

We have a full agenda planned for the meeting today. We'll start with hearing opening remarks from Admiral Rachel Levine. After Admiral Levine's opening remarks, we'll hear from Dr. Theresa Mullin, associate center director for strategic initiatives in the Center for Drugs, who will talk about FDA's patient-focused drug development efforts.

We'll then spend some time hearing from Dr. Hilary Marston, the chief medical officer of the FDA, who will provide us with a background on long COVID just to set the stage for the meeting.

We'll then move into our discussion with individuals who are living with long COVID and their loved ones and advocates. We have three sessions. Our first session will focus on the health effects and daily impacts of long COVID that matter most to individuals.

Our second session will focus on your thoughts about current approaches to managing long COVID. And our third session will focus on considerations when choosing whether or not to participate in a clinical trial, what are some of the things that make participation easier and what might make it harder. I'll better explain the meeting format and process right before we get into our first panel session.

Before we begin, I'd like to go over a few logistic and housekeeping points. This meeting is taking place in a fully virtual setting and is focused on hearing from people who have personal experiences with long COVID. Throughout the day, we'll have polling questions. You'll be able to answer those polling questions using a cell phone or any type of computer or tablet. We'll talk a bit more about that in a few minutes. In addition to the polling questions, you'll have the opportunity to share your experiences by either using the chat feature in the bottom right corner of the meeting screen or by calling the phone number that we'll be putting up on the screen throughout the meeting.

As I mentioned, we'll be taking calls throughout the meeting from people with personal experiences with long COVID. We're set up to take calls and receive comments in both English and in Spanish, so please share your experiences in either language.

One request that we have is that since the interpreters are simultaneously translating the meeting, if you do call in to speak with us, please try to speak slowly and clearly so the interpreters are able to effectively translate English to Spanish and Spanish to English. If we set things up correctly, you'll not hear the translation while you're speaking. This meeting is being webcast in both English and in Spanish. Captioning is available in both languages as well. The live webcast is being recorded. Both the webcast and transcripts of today's meetings will be archived on our website.

And with that, it is my pleasure to introduce Dr. Admiral Rachel Levine who will provide our opening remarks for the meeting. Admiral Levine serves as the 17th assistant secretary for health for the U.S. Department of Health and Human Services and is the head of the U.S. Public Health Service Commissioned Corps. She fights every day to improve the health and wellbeing of all Americans. She's working to help our nation overcome the COVID-19 pandemic and build a stronger foundation for a healthier future, one in which every American can attain their full health potential.

Admiral Levine's storied career first as a physician in academic medicine, focusing on the intersection between mental and physical health, treating children, adolescents and young adults and then as Pennsylvania's physician general and later as Pennsylvania's secretary of health. She addressed COVID-19, the opioid crisis, behavioral health and other public health challenges.

Admiral Levine, I invite you to turn on your camera and unmute your microphone, ma'am.

OPENING REMARKS

DR. LEVINE: Well, thank you very much. Good morning, and thank you for that kind invitation. And I'm very pleased to be with you today. It is truly my honor to hear from people with long COVID, their advocates and those that care for them. So thank you for the FDA for hosting this meeting.

In April of 2022, President Biden issued a memorandum and fact sheet accelerating the whole of government efforts to prevent, detect and treat long COVID, and he tasked HHS with hearing the charge. We convened our federal partners through the long COVID Coordination Council to facilitate this work, and we released two reports.

The first was the "Services and Supports for Longer Term Impacts of COVID-19" report. This is a plan that outlines over 200 federally funded supports and services for individuals experiencing long COVID and associated conditions and also mental health substance use issues and bereavement.

The second report was the "National Research Action Plan on long COVID," a plan that lays the groundwork for a comprehensive and equitable research strategy to inform our national response.

Since the publication of the reports in August 2022, we have continued to work with federal partners, including agencies such as the FDA. Most people who have COVID-19 recover quickly and completely. But some people continue to experience new, persistent and reoccurring symptoms or conditions for weeks, months or even years after the initial infection, and this has been termed long COVID. I think everyone here today is familiar with this concept of long COVID and have been drawn to this forum to share the ways in which long COVID has impacted their lives, whether as a patient, a provider, a researcher or an innovator. So thank you for being here today and thank you sincerely for helping us better understand what long COVID is and how we can help people.

Our driving focus is to ensure that everyone knows that long COVID is real. I'm going to repeat that one. Our driving focus is to ensure that everyone knows that long COVID is real. We want to help people recognize that if they have long COVID and they have the symptoms, that they should get care and support for their symptoms and their condition as soon as possible.

Earlier this month, we issued an updated fact sheet that detailed the progress that has been made towards the goals to prevent, detect and treat long COVID. In acknowledgment of the continued need for resources and supports, I visited Children's National Hospital Medical Center, and I visited their post-COVID conditions clinic in DC, where I heard from patients, I heard from children, from their families and their providers about the work that they're doing and the work yet to be done.

In the last year, I have traveled across the United States, stopping in cities such as New Haven, Kansas City and Richmond to bear witness to the impact of long COVID on individuals and their families, as well as the health care systems that seek to care for them. People living with long COVID, their families, their healthcare workers and researchers have shared with me the barriers in accessing treatment, from the barrier of providers that people have seen who don't believe that long COVID is real. Other barriers include long wait times for specialist appointments and the lack of treatment options for the variety of symptoms that people have. People I have seen and their families and their providers have implored us to do more and to start translating research into therapeutics so people can get the help that they need as soon as possible, to provide pathways to remission of symptoms and a pathway to recovery.

Providers have shown us that they do see patients improve. It's a very important point, always important to have hope, but it does take time. Foundational research is already providing valuable insights in informing the development of long COVID clinical trials. These clinical trials will help find the treatments that you need to help relieve the most challenging symptoms that people have. These clinical trials will test more than a dozen potential treatments. It is critical even in this moment, though, that knowing that you need help today, we need to listen to you. And we want to listen to you today. We want to learn from you, from your caregivers and from healthcare workers and all of those with lived experience.

Today, as the FDA hosts us in this virtual public forum, and as significant progress has been made towards the understanding of how to treat long COVID, we want you to help us take a step forward, one more step forward. We want to understand the symptoms that most impact your life, how you're treating them, what factors would you consider when determining whether you would participate in a clinical trial. And through this collaboration with you, we recommit to addressing the longer term impacts of the worst public health crisis that the world has seen in a century and to accelerate understanding and breakthroughs and to do that together, to do that as a partnership.

Beyond the winding down of the public health emergency for COVID-19, HHS will continue to address the needs of the long COVID community and continue to partner with patients, with states, industry, with advocates, with academic medical centers and more to ensure our commitment to protecting public health and wellbeing.

In the past year, we have made significant progress in the fight against long COVID through developing supports and services, through the research being done at the NIH, the CDC, the VA and more, we have made progress. But we are certainly not done yet. Agencies across the U.S. government continue to work together to conduct research to draw on the lived experiences of those with long COVID and of those who care for them and develop more supports and services. We want to provide opportunities to work together to disseminate information and resources, implement and support critical activities and to advance the science like today's FDA patient-focused drug development meeting.

So thank you again for hosting me. I appreciate your dedication, I appreciate your commitment and I appreciate your enthusiasm for convening in support of these public health goals. We know that long COVID is real, and events like today's allow us to answer your most urgent calls to action. I look forward to continuing to work with you, and I want you to know that your support is very important to me, Admiral Rachel Levine, the assistant secretary for health. It is very important to our secretary, Secretary Becerra and the work of this department as we all work together to improve the health of all Americans. Thank you.

MS. BENT: Thank you, Admiral Levine. Thank you and your office for working so hard with us on this meeting. We really appreciate it, especially given how busy I know you've all been.

I'd like now to invite Dr. Theresa Mullin to unmute and turn on her camera to provide us with a little background on the FDA patient-focused drug development program and on these patient-focused drug development meetings.

As I mentioned, Dr. Mullin serves as CDER's associate center director for strategic initiatives. She oversees areas of strategic interest to external stakeholders. She was instrumental in the creation of the patient-focused drug development program, and she leads CDER's international work. Dr. Mullin previously served as director of CDER's Office of Strategic Programs. Before joining the Center for Drugs in 2007, Dr. Mullin was assistant commissioner for planning in FDA's Office of the Commissioner.

Dr. Mullin, please go ahead.

OVERVIEW OF FDA'S PATIENT-FOCUSED DRUG DEVELOPMENT INITIATIVE

DR. MULLIN: Thank you, Robyn. Thank you so much for joining us today for this meeting. And as Robyn said, I'm going to provide you with a brief overview on FDA's patient-focused drug development initiative, And this meeting is part of that. And so, next slide, please.

So to begin with, what is FDA's role in medical product development and evaluation? Well, FDA has a broad portfolio, and part of our mission is to protect and promote public health by evaluating the safety and effectiveness of new drugs. And while we play a critical role in drug -- oversight of drug development, and that's one part of bringing products to market, FDA does not develop drugs or conduct clinical trials. Instead, our review divisions at FDA, for example, the Division of Neurology, Division of Psychiatry, Cardiorenal, many others, provide regulatory oversight of the drug development process and make decisions based on a review of the evidence that's generated in those studies, and on that basis, decisions about approval of new drugs and guidance to industry related to these matters. Next slide, please.

And so what is patient-focused drug development, or PFDD? Well, this is a systematic approach to ensure that patients' experiences and perspectives and their priorities and needs are captured systematically and incorporated into drug development and evaluation. And next slide, please.

This is really important to FDA decision-making. Patients are uniquely positioned, as we understand at FDA, to inform our understanding of the clinical context for drug review and regulatory decision-making. And by that I mean, what is the severity of this condition? What is it like to live with the condition and what treatments are available and how well are they working or not working? And prior to setting up this program, PFDD, the only mechanism we really had available to us to gather patient input were the sort of discussions we might have about a specific application in the context of an advisory committee meeting.

And only a few patient representative typically speak at those meetings, and there's a screening process, and so we don't really have a good opportunity in those settings to get the input from the full community of people experiencing a particular condition.

So these meetings, like the one today, give us a better way to more systematically collect that range of perspectives on the severity of the condition and what it's like and its impact on people's daily lives and their assessment of what's available and how well those treatments are working or not. Next slide, please.

So this slide is really meant -- I think that timeline is kind of pale, so you may not be able to see it very well, but this slide is conveying that the project, this effort began about 10 years ago. And in 2012, we had our first -- we set up this program. And from 2013 to '17, we really sort of made it a bit of a pilot effort and conducted 24 different meetings in different disease areas.

Oh, okay -- and basically this allowed us to -- there was so much interest in these meetings that we wanted to expand our ability to have them. And so we set up an externally led option here. And this is where patient groups lead the effort to set up and plan the meetings. And we assist them and we go to the meetings. We're able to join the meetings. And it's just been extremely valuable to us. Both the ones that FDA leads and the ones that patient groups lead really have given us a lot of important input. Next slide, please.

And this slide shows you just the range of conditions that FDA has and the ones that FDA has conducted. And I want you to note that literally 10 years ago today, we had our first patient-focused drug development meeting. And that meeting focused on chronic fatigue syndrome and myalgic encephalomyelitis. And that first meeting, we didn't know how it would go. We found it so powerful and it really made us realize how meetings like this can help us really understand. We're hearing directly from patients. And so in addition to the about 30 meetings that we've held, there have been over 80 meetings that have been conducted externally. And so this has really been a valuable opportunity for FDA and to listen and for patients to be able to share their perspective. Next slide, please. Next slide, please.

Thank you. So the format of these meetings is sort of a town hall style. We usually begin with an overview provided by one of the FDA doctors on the clinical background and currently available treatments, and that's followed by panel sessions. The first panel, typically we'll have a focus on symptoms and daily impacts that begins with having a sort of panel of patients and caregivers who provide a range of perspectives and share their experiences. And that sort of sets the stage for a broad facilitated discussion where we hear from everyone and we get the opportunity to hear from everyone who's participating in the meeting and wants to share what their experience has been.

That's followed by a session kind of similarly structured that looks at treatment options, and again begins with a panel of individuals' perspectives and what they've experienced to set the stage for that broader facilitated discussion. Next slide, please.

And so these meetings, each of them are tailored a little bit to the disease and the questions that may be of particular interest to try to understand better how we can develop treatments that are more effective and better for patients and maybe the issues around trials or other aspects of drug development.

And we have a wide range of participants, but we want everyone to remember that these meetings are really intended to hear directly from patients and caregivers. And so we're going to ask others to just remain in listening mode through these discussions so we can all benefit from hearing that perspective from patients, caregivers and patient representative.

After these meetings, we often have a docket that we'll open to receive further public input and comments, things people may not have been able to share or thought of during the meeting. We'll put that together with what we hear in the meeting and the recordings of the meeting to try to develop a very comprehensive report. We develop these reports called "Voice of the Patient" reports. And in fact, if you were to go to your favorite search engine and check into "Voice of the Patient" or patient-focused, you'll find the repository that we have there. But we want to have that report as a resource for future reference for our reviewers and for drug developers, patient groups and others. And with that, I'll conclude and thank you again for joining us today and look forward to hearing your perspectives today.

MS. BENT: Thank you, Dr. Mullin. I think it's clear from the number of people participating in the meeting today that patient-focused drug development and these PFDD meetings really play an important part in incorporating the patient voice into medical product development.

And now I'd like to ask Dr. Hilary Marston to turn on her video and, as soon as I finish her introduction, begin her presentation. Dr. Marston trains in internal medicine and global health equity at Brigham and Women's Hospital. Currently, she is the chief medical officer of the FDA. In this role, she serves as the primary clinical advisor to the commissioner and oversees the Office of Clinical Policy and Programs.

Before joining the FDA, Dr. Marston was senior advisor for global COVID-19 response on the White House COVID-19 response team. Dr. Marston has also served as the director for medical bio preparedness and response at the U.S. National Security Council and as medical officer and policy advisor for pandemic preparedness, focusing on emergency infectious disease preparedness and response at the National Institute for Allergy and Infectious Diseases at the National Institutes of Health.

Dr. Marston, thank you so much for joining us today. Please go ahead.

BACKGROUND ON LONG COVID

DR. MARSTON: Thank you so much for that kind introduction and thank you for the invitation to --

MS. BENT: Dr. Marston, I'm going to ask you to stop for one moment. We are having just a brief issue with the translation.

DR. MARSTON: No problem.

MS. BENT: Do we have the translation setup handled?

INTERPRETER: Confirming the Spanish interpretation has resumed. Thank you.

MS. BENT: Excellent. Thank you. Go ahead, Dr. Marston. I apologize for interrupting you.

DR. MARSTON: No apologies. That's so important. Thank you. Important to pause for that. So what I would like to do today is talk first about the terms and definitions; Next, go into some of the clinical features of long COVID, some potential causes, what we understand currently about epidemiology, the treatment options and regulatory challenges for drug development. And I think what you'll hear throughout this talk are a couple of emerging themes. Number one is we've learned a tremendous amount about long COVID.

But number two is that we have a ways to go in this area and that's why fora like today are so essential to progress in this area. Next slide.

So first, long COVID terminology. So long COVID is a patient-created and now widely accepted term. You will hear other terms that are thrown around in this space, but we have really been working to help coalesce towards this term with the leadership of patients. So other terms that you'll hear include post-COVID conditions, post-acute sequalae of SARS-CoV-2 infection, long-term effects of COVID, post-acute COVID syndrome, and more. But long COVID is the one that we're going to use for the purposes of today and indeed across the federal government. Next slide.

And this was actually quite intentional on the part of the federal government. So recognizing that patient-created term, the government built on that with a cross-HHS working group that sought to further define long COVID. And what we came up with is defined on this slide here. So I'm not going to read everything here, but the most important thing is that it's broadly defined and includes a wide range of signs and symptoms that continue or develop after initial COVID-19.

Importantly, it's likely not one condition, but it represents many overlapping different entities and likely they have different biological causes and that's something we'll go into in a little bit more detail. So this was the proposed definition shown on this slide and this has been a source of some ongoing discussion and indeed our colleagues over at the National Academies are looking at this definition in more detail, hosting a series of workshops. There's a link to those proceedings in the slide. Next slide.

So next, some of the clinical features of long COVID. So I said that it includes a range of symptoms. In fact, over 200 different symptoms have been reported. Most commonly they seem to cluster in a set of different areas. So first, brain, ranging from headache to brain fog. But there are also conditions such as stroke. Nose and nasal cavities, so this is one of the initial symptoms that was discovered quite early on when SARS-CoV-2 came to light, the loss of taste or smell and that's something that in some folks tends to persist. Lungs, this cough and ongoing shortness of breath. Heart, pounding heart and variable response to changes in activity. Skin, some people can get different sorts of rashes and bruises. And kidney, there's an increased risk of acute kidney injury, but often some ongoing effects on the kidney function. Next slide.

In terms of the possible causes of long COVID, there are a number of theories here and it's important to say that while we're learning quite a bit about long COVID, this is an area that we're continuing to understand. As I mentioned early on, there are likely some overlapping conditions that are encompassed within long COVID. Similarly, there are likely overlapping etiologies, causes that are actually leading to the symptoms that patients are reporting. So those causes likely include autoimmune conditions. Persistence of the virus is a possible cause, ongoing organ damage or results of existing organ damage and microclots. So microclots can exist in the acute condition but then can come up over time. Next slide.

In terms of how common that long COVID is, the range of estimates is wide, everywhere from 5 to 30 percent. Some reasons why you have such a large range, number one is the different symptoms and conditions being investigated. So it depends on how you ask the question. Similarly, the bounds of time that you use to define long COVID, so some individuals doing surveys are looking at three weeks after initial infection. Some people say many months. So again, that will dictate what you get in your results from a survey, where the study is asking the question, inpatient or outpatient settings, and how symptoms are assessed, whether it is self-report, drawing from an electronic health record database or formal survey.

There is a CDC Household Pulse Survey, which has some nice methodology behind it, that came up with an estimate of 6 percent. Worldwide, that estimate is about 65 million individuals globally. So this is, unfortunately, something that's being seen worldwide. Next slide.

Factors associated with getting long COVID. So first, a lot of these are similar to the predisposition to getting severe COVID. So, for example, having preexisting health conditions, having severe initial COVID-19 illness, lack of vaccination prior to SARS-CoV-2, there's some good evidence there and people who experience something called multisystem inflammatory syndrome during or after COVID-19. So multisystem inflammatory syndrome is where different parts of the body become inflamed that include many different parts of the body, from the kidneys to the brain, skin and the gastrointestinal organs. And just as it did with initial COVID-19 infection, health disparities are unfortunately rearing their ugly head when it comes to long COVID as well. And that's something we would like to hear more about.

Long COVID in children. So just as there are uncertainties about the prevalence of long COVID in adults, although it's quite clear that it is very common, long COVID in children estimates range quite a bit as well. The symptoms and natural history, some overlap with what's seen in adults and some do not. So this is something that certainly merits further research. Sorry. I'm behind. Can you go forward two slides? Thank you. One more. Thank you.

So, in terms of treatment options, so there's no FDA approved drugs or authorized treatments for the treatment of long COVID. For most patients, the goal is going to be to optimize their function and their quality of life. So that's why meetings like today are so important, so that we understand what is most important to patients in terms of those measures. Symptom management approaches, therefore, might be very important here. And management is going to change as the evidence emerges. And we hope that that will happen because it means that we're developing new, better approaches. Next slide.

There are many challenges, though, when it comes to drug development. So first is that it's a new entity and we're continuing to understand it. That includes just the epidemiology of the disease. So designing studies, it's really important to understand how common that a condition is. Second, again, there's this heterogeneity, this diversity in the symptoms that people are reporting, and it might indeed be multiple overlapping conditions. That makes it, again, challenging to study and understand if your treatment is having an effect. And then the tools for how we assess how a treatment is working, we want to make sure that those tools are accurately reflecting how patients feel, because again, what we want to be developing in treatments are treatments that really impact the symptoms that the patients are seeing. Next slide.

And one point that is important to make here is that our colleagues over at the NIH have been funding a series of studies under the Recover initiative that is working to both understand the natural history of disease, but also the effectiveness of interventions.

So, in conclusion, long COVID as a post-viral condition can be very severe and disabling, but present with diverse symptoms and symptom clusters and with several potential biological causes, likely multiple overlapping conditions. There are a number of challenges associated with drug development, but FDA is committed to supporting drug development for long COVID along with our federal partners. And in this, it is essential that we have the patient's voice front and center.

So to that end, thank you so much for your attendance here today. We really appreciate it, and we look forward to engaging in the discussion today. Thanks.

OVERVIEW OF DISCUSSION FORMAT

MS. BENT: Thank you, Dr. Marston. I think that this is really helpful for us to have this presentation to set the stage for what we're about to hear from our panelists and meeting attendees who have lived experiences with long COVID.

Moving on, I'd like to share with you all a bit more about how the meeting will proceed. It's been truly an honor to work with the panelists that you'll meet in just a moment as we prepared for today's meeting. And thank you to Admiral Levine and Drs. Mullin and Marston for the very informative presentations that give us some context to think about during this next part of the meeting that really is really all yours.

If you're new to this area of what FDA does and what patient-focused medical product development is, then I hope that we gave you just a little bit of a background on that and especially some of the key terms and words that we'll be using today.

Before we get started on this next part, where those of you with lived experiences with long COVID are really the main participants, I just want to share a little bit of information, kind of an orientation to build on what Dr. Mullin talked about to help you understand the meeting structure and why we've set it up this way, because it's intentional.

Those of you who are here representing yourselves or your loved ones with lived experiences with long COVID, you are the experts. And the expertise that you have is what we're all here to hear about today. We've kind of flipped the script, so to speak, on the type of meeting that most of us go to, where you have a lot of medical professionals giving presentations and having discussions while everyone else listens. Today we've reversed that. We've heard some opening remarks from experts in their field, but you are experts in your field. You're the ones who know what long COVID is like to live with.

So our goal today as we start this discussion portion of our meeting is to really foster an open dialogue on personal experiences and perspectives on long COVID. Our three main topics for discussion are health effects and daily impacts of long COVID, followed by current approaches to treatment, followed by considerations for clinical trials.

We'll start each session with a panel of individuals with long COVID. There are six panelists for our first topic. After hearing from the panelists, we'll broaden the dialogue to include other individuals and family members who are joining us on the webcast. Anyone who's watching the meeting who identifies as a person with long COVID or a family member or loved one is welcome to participate.

Aside from panelists, we don't have anyone else identified to speak, so we need you to share your experiences in order for this meeting to be successful. The purpose is to build on the experiences shared by the panel, and I'll ask a number of follow-up questions. Throughout the day, polling will be done via computer or cell phone, and as I mentioned previously, we're taking comments from online through the meeting chat feature and via telephone if you've got something to add.

So this is your opportunity to build on the information shared by panelists. So we really hope that you feel kind of the importance of your participation in the meeting today, to have your experiences and priorities heard, not only by the FDA and others in the federal government, but from representatives from medical product developers, researchers, clinicians about long COVID and what you'd like to see happen to help those with long COVID.

So please take this opportunity, and we hope that this will be your invitation to participate with us in the discussion. We encourage you to call in via phone to share your comments when speaking. You can remain anonymous. I mean, you don't have to give us your first name you're your last name. You may state your full name if you want. But really mostly what we care about is you're your experience is.

When you call in, there are a couple of things that will help us. One is if you stay on the topic that we're discussing, whatever topic we're talking about. If we're talking about symptoms or if we're talking about daily impact, it would be helpful if you could think about the topic and stay as close as possible to that topic. It's also helpful if you can keep your points to about two minutes and focus really on one or two things that are particularly relevant to you so that we can go on to as many people who want to speak as possible.

For transparency, we request that at the time of your first comment, you disclose if you are affiliated with an organization that has an interest in long COVID, or if you have significant financial interests in long COVID drug development. If you're submitting comments via the webcast, you can provide whatever name you'd like. Please don't worry about us being overwhelmed by comments. We can handle it. We'll try to summarize them as much as possible. We'll do our best to share the comments we receive via the Web platform. But if we're not able to read all of the comments out loud today, your comments will be incorporated into our final summary report.

One thing that is very exciting about our meeting today is that we've had more than 1,400 people registered to participate. Of the people registered, over 850 of you are either people with long COVID or loved ones or patient representatives. Now, we are grateful, very grateful to the long COVID community for their support of this meeting, but we also realize that there may not be enough time for everyone who wants to share their experiences today to do so.

As Dr. Mullin mentioned earlier, we have a public docket for this meeting that will be open until June 26th of 2023. We encourage you to share your experiences and expand upon what we discussed today through the public docket. The comments will be incorporated into our summary report as well. Anyone is welcome to comment through the docket, whether you're joining us via the Web on this meeting or whether you know someone who wasn't able to participate today, but you think they have something to contribute. Please encourage them to submit their comments. You'll find a link on the slide here, and we'll also email this link after the meeting to everyone who's registered via the event website. You can submit your comments to the docket as anonymous as well.

And I want you to keep in mind that if you do submit to the public docket, that word public is in there for a reason, and this will go onto the website. So please think about how much personally identifying information you want to share. We don't need that information. We care about what your experience is, so please keep that in mind. You can just say anonymous, anonymous, or leave the parts empty when we ask what your name is.

There are also just a few ground rules for today's discussion. We're here first and foremost to listen to those with long COVID and their loved ones. We'll try to accommodate all of those who want to speak. We're happy to see a number of people who represent research and medical product development registered for this meeting. We believe that the input we hear today will be important to you as well. We just ask that you stay in listening mode.

FDA staff is really here to listen as well. We know that you may have questions about medical product development or drug review. If you have specific questions, we encourage you to share them with us via email. Our contact information is on the meeting website. We'll get back to you with more information following the meeting.

As has been described, our discussion today is focused first on the health effects of long COVID and daily impacts, then approaches to managing those health effects and then clinical trial participation. Our discussion may touch upon scientific treatments. However, the discussion of any specific treatments should be done in a way that helps us to understand the broader issues, such as what health effects are being addressed and how that is meaningful to individuals with long COVID and their loved ones.

Our discussion is going to focus again on health effects and treatments. We know that this is a very complicated issue and there are many concerns and many questions you have and things that you have to think about when living with long COVID and getting the support you need. All of those are important. However, today we hope to focus on the topics that FDA needs the most input on so that we can best fulfill our role regulating medical products and facilitating medical product development.

And so, while you take in this next slide, which outlines how to actively participate in the meeting, I'd like to take the opportunity to ask my FDA and HHS colleagues to turn -- on the panel to turn on their video and introduce themselves. And we'll start with Dr. Karimi Shah.

DR. SHAH: Thank you, Robyn. Good morning. My name is Bani Karimi-Shah. I am the deputy director of the Division of Pulmonology, Allergy and Critical Care here at FDA, and I'm very excited to hear what you all have to say during today's meeting.

MS. BENT: Thank you. Dr. Senatore?

DR. SENATORE: Good morning. My name is Fred Senatore. I'm a lead physician with the division of Cardiology and Nephrology at the FDA. And I'm excited to be here, and I'm looking forward to learning from the patients who've experienced long COVID. Thank you.

MS. BENT: Thank you. Dr. Habal?

DR. HABAL: Hi. Good morning. My name is Nadia Habal, and I'm an acting clinical team leader in the Division of Rheumatology and Transplant Medicine at the FDA. And I'm also a practicing adult rheumatologist, and I'm looking forward to this meeting. Thank you.

MS. BENT: Dr. Sullivan?

DR. SULLIVAN: Hi. My name is Shannon Sullivan. I'm an endocrinologist, and I'm a clinical team leader in the Division of General Endocrinology at FDA.

MS. BENT: Thank you. Dr. Stabinski?

DR. STABINSKI: Hi, my name is Lara Stabinski, and I am a medical officer in the Division of Antivirals. I'm also a practicing infectious disease clinician.

MS. BENT: Thank you. Dr. Connolly?

DR. CONNELLY: Hi, my name is Mark Connelly. I'm in the Office of Vaccine Research and Review. I'm a medical officer, and I wanted to thank everyone for sharing their experiences.

MS. BENT: Thank you. Dr. Weltz?

DR. WELTZ: Good morning. My name is Adam Weltz. I'm a board certified general surgeon, practicing clinician, associate professor of surgery in Annapolis, Maryland. I am also a medical officer in CDRH, which is Center for Devices and Radiological Health, a medical officer on the team that reviewed many of the infection controlled devices during the pandemic.

Looking forward to hearing your stories today.

MS. BENT: Thank you. We also have Dr. Marston. I know I've introduced you, but if you want to briefly just say hello again.

DR. MARSTON: Hello. Just glad to be here. Thanks so much.

MS. BENT: Thank you. Admiral Iademarco?

DR. IADEMARCO: Yes. Good morning. Good afternoon, everyone. I am Michael Iademarco. I am the deputy assistant secretary for health for science and medicine in the Office of the Assistant Secretary for Health with Admiral Levine. And together we're leading the long COVID coordination across 14 federal government departments. And I am a pulmonologist and ICU physician, spending most of my career in public health.

MS. BENT: Thank you. Dr. Soake Adams? All right. Dr. Patel?

DR. PATEL: Good morning, everyone. My name is Priti Patel. I'm a senior advisor for post-COVID conditions at the Centers for Disease Control and Prevention. I'm an internist by training and really appreciate the opportunity to be here as part of this meeting today.

MS. BENT: Great. Thank you all. You are welcome to turn off your video if you would like at this point. So from time to time during our meeting, we will turn back to our FDA panelists to see if they have any follow-up or clarifying questions about what we just heard from our other panelists.

I also want to introduce my colleague, Shannon Sparklin, who will be keeping an eye out for comments that come in through the Internet. She will be backed up by Ethan Gabbour. Shannon will be sharing the comments throughout the meeting. She'll also be coordinating with our other colleagues, Lena Marzouk, Will Lou Allen and Steven Ganache, who you'll speak to if you call in to provide comments on the phone. Shannon?

MS. SPARKLIN: Good morning. My name is Shannon Sparklin. As Robyn mentioned, I will be reviewing the written comments that we received through the webcast and summarizing them. Thank you.

MS. BENT: I see that I muted myself. It's only three years into the pandemic. So we will have some polling questions today, and we're using a third-party application, Mentimeter, to run our polling. Polling on Mentimeter's site, menti.com, is anonymous and can be done via cell phone or on your laptop or tablet. Please note that we're not tracking individual people's answers. We'll only see the responses grouped by option.

You can access the Mentimeter poll in two ways. You can use your cell phone camera to view the QR code on this slide, which will take you to the survey, or you can go to www.menti.com and use the digital code on the slide to enter the survey. It sounds like maybe we're having some issues with the Mentimeter, so we will work on that and we will get that going shortly. Unfortunately, the polling is also only available in English, but I will read the polling questions and answers so that they will be translated.

And so with that, let's begin with a polling question. I hear that it is working again. So please get your cell phones or computers ready. All right. Question one. We're starting with some basic demographic questions so that you can get familiar with the polling platform. And so the first question is where do you live. Option A, within the Washington, DC metropolitan area, including the Virginia and Maryland suburbs; option B outside of the Washington, DC metropolitan area.

And so while you're completing the polling questions, I'm going to share with you one of the challenges of the virtual setting. There is a little bit of a lag between when we speak here on the backend of the meeting and then what is broadcast to the meeting participants. That lag time can be 15 to 30 seconds. So you'll see the answers for polling kind of trickle in. For some questions, you'll have one answer. For others, you may have multiple answers. These polling questions are meant to be a discussion aid for today. They're not a scientific survey.

So let's see. All right. It looks like everything is working and we're getting responses. I don't see a lot of challenges with the application. It seems like it's starting to work, and it looks like this is one of the benefits, I think, of having the meeting in a virtual platform. We really do have a large number of participants who are able to join us from outside of the metropolitan DC area. And for that, we're very grateful because really kind of understanding the experiences of people throughout the country and even more broadly throughout the world is really important and helpful.

So let's move on to the next question. Next question, are you or a loved one currently experiencing symptoms of long COVID? A, yes; B, no. All right. Once again, it looks like we're getting some good responses, and we are seeing what we would anticipate from our registration, which is that a majority of the people that registered have had personal experiences through their own or their loved ones long COVID. And so from this point on, we'll ask that each polling question be answered only by an individual living with long COVID or someone who is answering on behalf of a loved one with long COVID.

So let's move to the next question. Okay. Here we go. What is your age? Remember, if you are answering for a loved one, please answer with their age. The options are A, 0 to 10 years old; B, 10 to 17 years old; C, 18 to 29 years old; D, 30 to 39 years old; E, 40 to 49 years old; F, 50 to 59 years old; G, 60 to 69 years old; and H, 70 years or older.

All right. And we're getting a good number of responses, and it looks like a majority of our participants today are kind of in that 30 to 60 year age range, with most of our participants being -- it's changing, so most of them being 40 to 49 years old, but just slightly over the 30 to 39 years old. And so I think that this is maybe what we were thinking we would see based on the registration as well.

So let me now move on to our next question, which is, do you identify as, A, female; B, male; or C, other? All right. So it looks like we have a majority of female participants at the meeting, but it does look like we have a good representation from males as well. So thank you all. It looks like we have a range of people participating today, all age ranges from across the country. And that's really great. That's what we had hoped for.

We have just two more questions, and these are going to kind of delve a little bit. We're going to stop asking about demographics and really try to start understanding your experiences with long COVID. So we'll move on to the next question, which is what parts of your body are affected by long COVID? And for this, you can select all that apply, that includes, A, muscles and joints; B, heart; C, lungs; D, brain and nervous system; E, kidneys; F, liver; G, digestive system such as stomach and intestines; H, blood; or I, other, such as mouth, nose, hair, et cetera.

Okay. So we're seeing a lot of muscles and joints, brains and nervous system, and a good amount of other. And so it seems like we're seeing our participants today experiencing issues with multiple parts of the body that are affected by long COVID. And so we're going to hear a bit more about people's experiences with long COVID in just a minute. For those of you who have selected other, I would request that you think about calling in a bit later to share what you've experienced.

And so finally, thanks everyone. We're going to have just one more question before we move on to our first panel discussion. And that question is which type of healthcare providers are you seeing for your long COVID symptoms? And you can check all that apply. We have, A, primary care provider. This could be an internal medicine provider, a family practice provider. It could be a pediatrician or a pediatric nurse practitioner if you are answering for your child; B, long COVID specialist or clinic; C, medical specialist. This could include specialty care outside of a long COVID clinic. It would include pulmonologists or cardiologists or other specialists; D, chiropractor or complementary healthcare provider; E, other; or F, none of the above.

So it looks like we have a number of people really working with their primary care providers as well as medical specialists. And about 18 or 19 percent -- oops, it's dropping, 17 percent being seen in long COVID clinics. All right. So thank you all. I think this is really helpful information. It'll be great as we kind of move into our conversations after we hear from our panel.

But now we're going to move right into hearing from our panelists. So now, as I mentioned previously, topic one will focus on the health effects and daily impacts of long COVID. And we have six panelists who will start off the session by sharing their experiences. In about 30 minutes, when our panelists are done sharing their experiences, we'll move into the interactive portion of the meeting by asking you about your experiences. If you hear something from our panelists that really resonates with you or if you want to share a bit of your experience, please consider sharing your comments via the Web or closer to the end of the 30-minute period around 11:30 Eastern time. Maybe give us a call to share.

You should also know that if you call in and are placed on hold, the hold music will not be music. It will be the English version of this meeting. So you won't miss out hearing from our panelists if you call in to speak. We will ask you to mute the device you are listening to the meeting on just to prevent there from being any audio issues. If you are Spanish-speaking, you may continue to stream the meeting. But we ask that when you are notified that we will be taking your call, you mute the speakers on your device that is playing the meeting.

And with that, we're ready to turn to our panelists. I'd like to start by inviting Jill to share her experiences with long COVID. So Jill, if you want to turn on your video, which you have on, and unmute, thank you so much for being here. And really thank you for being our first panelist.

TOPIC 1: HEALTH EFFECTS AND DAILY IMPACTS

MS. ANDERSON: Thank you, and good morning. My name is Jill Anderson and I would like to speak to you today about my experience with long COVID. I initially became acutely ill with COVID November 7, 2022. Shortly after the resolution of my acute illness, I began to notice lingering symptoms and new symptoms that were not present during my acute illness. Today I would like to focus on a few key symptoms out of the many I endured and continue to experience.

One of the initial symptoms I noticed was significant brain fog. I was having difficulty concentrating, thinking clearly, and my memory was so impacted that I was legitimately concerned for my cognitive functioning. Simultaneously, my vestibular system was also impacted. I never had vertigo, but suddenly I was constantly dizzy. It felt like my brain was banging around in my skull. I was off-balance. I could be standing, and then all of a sudden I would just lose my balance. I would get up in the middle of the night and take a step out of bed and fall to the floor. It was terrifying how my world was spinning and out of balance, and I could not recall pertinent information or complete sentences when trying to articulate in conversation.

Additionally, I was experiencing significant fatigue that was worsened by my brain working overtime to compensate to the changes to my vestibular system and cognitive dysfunction. I also lost my appetite for about three months, and it continues to come and go. This was coupled with repeated bouts of severe IBS flares that cause pain, cramping and bowel irregularity.

So far I've lost close to 20 pounds and I weigh about 102 or 103 pounds currently. Prior to COVID, I was training for a 10K and two 5K races. About a month or two after my acute illness, I started noticing my heart rate changing from a very low rate to racing upon standing. This led to a diagnosis of postural orthostatic tachycardia syndrome, or POTS. POTS is an autonomic disorder and symptoms such as exercise intolerance, headaches, fast heartbeat, dizziness, GI issues, shortness of breath and numerous other symptoms are associated.

All of these symptoms discussed I continue to experience. However, they significantly ebb and flow, and every day I wake up and I have no idea what kind of day I will have. I work hard to avoid post-exertional malaise or what I refer to as a crash where I'll push myself too hard mentally or physically, and this will exacerbate symptoms and trigger a two-week migraine or a two-week IBS flare, or I'll be too dizzy to leave my couch for days. Other days I'll get glimpses of symptom improvement, but those are limited.

All these symptoms continue to have an impact on my current employment. I'm a director of all the emergency and acute behavioral health services for a community services board in Virginia. My programs are responsible for the safety of the community and the individuals we serve. My career requires multitasking, quick thinking and decision-making and the nature of the work is intense and requires sound risk assessment. I'm on call 24/7, 365 and the role requires in-person attendance as well as direct client intervention when necessary.

I'm currently on intermittent FMLA, work mostly remote and work a reduced schedule due to my symptoms. I worry if I'm unable to meet my job expectations due to my -- my job expectations due to my cognitive deficits, fatigue, ongoing migraines and GI issues, continued need for remote work, continued crashes, that I could be moved to a different position or lose my job. I've worked in emergency services and crisis work for my entire professional career of 15 years, and this job is incredibly important to me. Not being able to keep up with the demands of this job over the past few months has been devastating. Thank you for your time.

MS. BENT: Thank you, Jill. Thanks for being the first one to speak and being brave enough to share your experiences with us. There's certainly a lot there and we really appreciate you sharing that. We're now going to turn to Heather-Elizabeth who is going to share some of her experiences with us.

Heather-Elizabeth?

MS. BROWN: Thank you so much. Good morning, everyone. My name is Heather-Elizabeth Brown. I am a bivocational minister and corporate trainer in Detroit, Michigan. Currently, I serve as a patient representative and committee leader with the Recover initiative with the NIH. I am also a long COVID advocate, COVID survivor and clinical TRIUMPH participant with long COVID research and awareness.

I contracted a very severe case of COVID in April of 2020 during the first wave when there was limited information and limited effective interventions.

I contracted COVID-induced pneumonia in both of my lungs that resulted in me being placed into a medically induced coma and onto a ventilator for 31 days from April 18th until May 19th of 2020.

Although I had many complications during this time, including having a stroke, blood clots and bleeding issues, I did survive by the grace of God. And very quickly after I began developing symptoms of long COVID, things that had not presented themselves in my initial infection and started to present themselves maybe as early as a month or two after I first was discharged from the hospital.

My lived experiences with long COVID cannot be overstated or overemphasized. In every area and every facet, my life has been impacted. After my initial hospitalization, I continue to deal with several long COVID-related issues today. The ones that are still very prevalent and that I still struggle with include brain fog, extreme fatigue and residual emotional challenges, including PTSD. And as a long COVID patient and a survivor, I can definitely say that every major system in my body has been affected by long COVID. That includes my nervous system, from my skin to my hair, my reproductive system, digestive, lymphatic, endocrine, any system you can name has pretty much been affected.

And long COVID has not only affected my life, but the lives of my family, my friends, my elderly parents and my brother who have had to sacrifice so much to continue to support me during the seemingly never-ending journey.

Before COVID I was serving as a chaplain with the Detroit Police Department. I was very active in several ministries in my spiritual community, and I really enjoyed being outside and walking and taking hikes and doing anything active. However, over the past years, there have been several serious long COVID-related complications and symptoms that I have developed that have presented particular challenges when it comes to my health.

Over the past three years, I developed COVID-induced diabetes, which necessitated me taking three to four insulin shots every day for almost a year. I was not diabetic before I contracted COVID. I also developed COVID-induced high blood pressure that necessitated at least two different medical leaves of absence from my employer because of the challenges that those faced. I also had blood clotting issues, which did result in blood clots and a stroke, which I mentioned earlier. And after my initial infection, I've struggled with everything from lymphedema, loss of breath support, fatigue, and again, the brain fog.

So I have been lucky that in terms of my limitations and the struggles that I have had with long COVID my employer has been incredible and has done as much as can possibly be done in order to create accommodations and opportunities for me, especially during the first two years when I was having appointments and anything from physical therapy to medical or specialist appointments anywhere from three to five times every week.

These continuing issues have definitely severely affected my career and my career trajectory. Although I do now work a hybrid schedule and I do have accommodations, I do still face challenges. Brain fog has been one of the notable ones, especially because as a trainer, my entire business is teaching and training and communicating, so having moments of not remembering what I was talking about, as you can see, could be very challenging.

Over time, I would say that my long COVID symptoms have ebbed and flowed. Some have lessened and some have persisted. I would say that obviously the major ones, including the diabetes and high blood pressure, have been the most challenging, and I have seen steady improvement. However, other issues, such as the brain fog have necessitated that I have had to seek out different treatment options in a variety of ways, whether it's with the University of Michigan Long COVID Clinic. I had a complete neuropsychological evaluation, brain scans, MRIs, appointments with different neurologists and specialists, and I've tried traditional and nontraditional treatments, everything from functional medicine to natural remedies, acupuncture, sound bathing. I've pretty much tried everything that I can think of or that I've seen on the Internet in order to find some relief.

So I am very thankful for this opportunity to be here before you and to share my experience with the other people who are dealing with the daily impacts of long COVID. And I definitely think that this is a very important conversation and I am thankful for this opportunity in this platform and everyone who is participating in hopes that we can continue to move forward, continue to find research and continue to find a resolution for all of us who are suffering. Thank you very much.

MS. BENT: Thank you. Thank you so much, Heather-Elizabeth. I suspect that many of the experiences that you mentioned are going to resonate with a lot of our meeting participants as far as the symptoms go, and we're going to touch more on some of these topics during the follow-on discussion.

Now, Linda, we're going to ask you to turn on your camera and share your experiences with long COVID. So please go ahead.

MS. VARNO: Good morning. My name is Linda Varno. I am a pediatric long COVID advocate whose husband and child, my son, are both experiencing long COVID. I'm also the co-founder of Team Varno, which is a personal blog dedicated to the care of a child with long COVID. Thank you for the invitation to participate today.

For the past 751 days, my 14-year-old son, Aidan, has been experiencing effects of pediatric long COVID. Aidan's symptoms, which have been documented on our Team Varno Facebook page, began four and a half months post-COVID infection. Even with multiple PCR tests, Aidan did not have a positive result. However, blood work taken at the time showed that he did have COVID antibodies. For the past two years, Aidan has experienced severe, excruciating, amplified pain that is centralized to his lower right back and will diffuse throughout his entire body. The pain, which does not respond to pain relief medications, becomes so severe that Aidan will experience nonepileptic seizures. Additionally, he frequently loses control and function of his body, which impacts his mobility.

Aidan has difficulty thinking, decreased executive function, fatigue, heart palpations, blood flow problems, intermittent loss of speech, trouble sleeping and is starting to forget what it was like to not be in excruciating, unrelenting pain all day, every day. These symptoms affect Aidan's quality of life and his fluctuating care needs. Aidan now has a silo effect in his medical chart, which includes over 12 different diagnoses and multiple medical specialties.

His symptoms also ebb and flow, especially with weather changes, and no two days of symptoms over the past two years have been identical. The extreme pain, brain fog, fluctuating mobility, intermittent loss of function, lack of public awareness and lack of financial support are some of the significant impacts pediatric long COVID has waged on Aidan and our family.

Parents like me are having to quit their jobs to be full-time caregivers and do not have caregiver or supplemental financial support. The insufficient understanding and compassion from the medical community, access to quality care and options available to patients and their families is limited. Currently, Aidan is receiving care for his amplified pain at a neurorehabilitation clinic that is 15 hours away from home and 100 percent out of pocket. This is the reality of what families across the U.S. are doing to help their children get better. Anything.

A specific activity that Aidan cannot do as fully as he used to is his schooling. The mental fatigue, academic requirements and attendance laws have been huge hurdles for someone with medical documentation of symptoms that ebb and flow. Even with accommodations and parents who genuinely care about his education and future, he is struggling. These kids are truly fighting for their lives. It's not an exaggeration.

Mental health care and pediatric patient support groups are needed for pediatric long COVID patients, their siblings and families, more than you know. Being part of a caring community matters.

Lastly, I want you to know that millions of children experiencing pediatric long COVID, whose disabilities, both visible and invisible, along with their families, are suffering, experiencing unimaginable trauma and are counting on your help. We are clinging to hope. Thank you.

MS. BENT: Thank you, Linda. Thank you for being here and for sharing Aidan's story. I know that he had given you permission to share his story and we really appreciate hearing what it has been.

MS. BENT: So now we're going to turn to Estefania. Estefania, please go ahead and share your experiences.

MS. OTERO: Thank you for the invitation to talk about my life with long COVID. I'm 52 years old, I live in Spain, and in January of 2021, I had COVID. I didn't vaccinate. I'm a doctor. The impact in my daily life is complete. I denied it in the beginning, and I was depressed and I needed help. And during these two years, I've learned to live with the disease. I've learned to organize my days and to avoid physical and mental fatigue as possible. This implies physical training in the mornings to recover my muscle mass and maintain it. I sleep for two hours or whatever is necessary to study or to read in the afternoons. And I'm lucky to have a husband and children who are grownups, who help me and have supported me throughout the process.

The symptoms have evolved over time and they have improved regarding intensity. Physical fatigue, it was overwhelming. I lost almost all the muscle mass. But once I recovered it, it still doesn't work. I have many limitations and I have to distribute it consciously. And I have pain. I used to run half marathons. Not anymore. I have a different pain. It's a very intense pain that is not related to previous activity. Brain fog has improved. I'm able to read more. For many months I didn't remember anything I read and this produced anxiety. And I only listened to music or read simple things. I still train on this, assuming that I forget many things I learn. For instance, if I'm interested in a medical issue, I make slides about it, although when I see them, I do not remember I made them.

Brain fog and physical fatigue prevent me from doing my previous work as an ER physician because I might not remember something quickly so as to treat my patients despite I have all the information in my cell phone. And also they are not able to go quickly to the third floor without a lift and not even walk through a hill or to do prolonged resuscitation. I'm in medical leave and I'll see if I am able to go back to work as a doctor.

This has also affected my personal life. I can't have a spontaneous life anymore. Now I have to plan and have a plan B just in case I have a bad day and I sleep little. I can't be out with friends late. I do not go to clubs anymore and, well, we go out at noon. Well, you can't stop living. You have to enjoy. It's very hard. But we are survivors of COVID and we have to make the most out of it. And that's it. Thank you very much everyone, and I encourage you.

MS. BENT: Thank you, Estefania. We're really hearing a diversity of experiences with some very common themes. And so for our next panelist, we're going to hear from Katie who's going to share her experience.

Before we hear from Katie, let me just ask our panelists to speak slowly so that the interpreters are able to capture the full text of what you are saying. So Katie, thank you so much and please go ahead.

MS. DRACKERT: Hello, everybody. My name is Katie. I'm an artist, a first generation college student, a friend to many and a daughter to my sweet parents. Before long COVID, I was a dancer, practicing for at least 45 minutes at a time and taking on gigs that required hours of stamina. After a year and a half of long COVID, I still don't feel confident reclaiming my dancer title. Summarizing one of the most painful chapters of my life into a few minutes is difficult, but I will give it my all in hopes of furthering an accessible recovery process.

Fatigue mixed with brain fog has been one of the most debilitating symptoms. The silent and invisible symptom has created a negative domino effect in my life. They are as follows: struggling with basic care such as cooking, not being able to keep or find accommodating jobs, inability to read without quickly tiring, falling behind in school, leading to dropped classes. Dancing pushed me into fatigue spells that lasted for days, shelving my art career. A negative impact on my personal relationships. Muscle loss due to being sedentary, causing my hypermobility issues to worsen, leading to more injuries. A need for more doctors' appointments, which creates more medical debt. High stress due to financial instability, thus worsening the fatigue. And the financial stress has been so strong from my lack of ability to work that I actually experienced food insecurity for the first time.

I often find that those who have not experienced fatigue struggle to understand what it is like. So I created some imagery. It's as if your inner dialogue becomes full of static, making it difficult to sort through your thoughts without further exhausting yourself or fatigue is like a phone that has been charged all night long only to drop to 10 percent after one call, which I think a lot of us have maybe experienced, and I just don't want this symptom to be underestimated.

Next is depression. My friends would tell you that prior to long COVID, I managed anxiety, not depression. I was a person fueled by hope. I was anxious, but I was definitely hopeful. The long COVID-fueled depression dissolved my hope. It furthered the negative impact on my personal relationships. I could no longer feel joy, purpose or motivation. I would have very excessive crying spells out of nowhere, sleep issues and suicidal ideation. All of this made it harder to find an accessible job, school more difficult and further fueled the fatigue.

Before my second COVID infection, I thought I was experiencing pure grief. I didn't experience the full-blown effects of this deposition until around six weeks after my second COVID infection in May of 2022. It felt like a switch had flipped in my brain and I knew what was logistical and I knew that hope existed, but it didn't exist within or around me. The severity nearly put me in an inpatient program and I could not pull myself out of this depression alone. It required intervention from friends, my therapists and doctors.

And finally, it worsened my preexisting medical issues. Prior to long COVID, I knew it was likely I had endometriosis, but at least it was somewhat mitigated with over-the-counter treatments. And once long COVID came into the picture, my period pain was so debilitating that I went to the emergency room twice. They gave me prescription pain medication and that did little to nothing. My cycle became excruciating for 25 days out of the month, and once again, long COVID stood in between me and bettering my future. It made my asthma and my allergies much worse. Before my infections, I only needed an inhaler when I experienced a common cold, and now I need it on a regular basis. And at times I require a nebulizer.

Asthma and allergy issues made it difficult to complete daily tasks. The shortness of breath I experienced on a consistent basis was absolutely horrifying. Simple things would cause shortness of breath, and as a dancer, this completely broke my heart.

I hope we can all work together to find sustainable solutions for us and relieve the isolation that long COVID has brought into our lives. I hope listening to us today fosters empathy for the dire need for treatments. Thank you so much for caring enough to show up today. And thank you for taking the time to listen as to how long COVID has changed my life.

MS. BENT: Thank you, Katie, for sharing your experiences. And our final panelist for this topic we're going to hear from is Sudeepti K. So let me ask Sudeepti -- you already have your camera turned on. Excellent. And please go ahead and share your experiences.

SUDEEPTI K: Sure. Thank you for having me and thank you for everyone that has put this long COVID day together. I'm sure as you're hearing through the experiences here today, some of us patients who have been going through this really appreciate the strides that FDA is making in this direction to make our voices heard.

So prior to contracting COVID, I was a very healthy 30-year-old. I was very active around the house, had a very busy social schedule, had vacations planned and weddings and a very active lifestyle. I contracted COVID in June of 2022 and the day I tested positive and went to go get a positive test at the local urgent care, they noticed that my blood pressure and my heart rate were a little high. But they said that that was pretty common with folks that are dealing with an acute infection of COVID. They did an EKG to make sure my heart was okay and said that some of the chest tightness should subside after the acute infection.

So as I went through the infection, I would say I had a mild to moderate case of COVID at the time. And after I tested negative, I started noticing that my chest tightness wasn't fully going away and my heart rate wasn't fully back to normal either. It just kind of continued resting. And then I had what I now call as a high heart rate episode where I could either be active or completely resting, sitting on my couch, and my heart rate will suddenly shoot up to like 190 or 200 and typically deep breathing will bring it down. But the first time that happened, I also had shortness of breath, my oxygen had dropped and it was a very scary episode to experience for someone that has never had any other health issues prior to getting COVID.

So I was put on a beta blocker for these symptoms. But as kind of the weeks went on into July and August, I noticed that I was having persistent chest tightness going up into the neck region that where my sore throat during COVID was the worst is, to this day, a sore spot for me. If I drink a warm beverage, I can feel exactly where the sore throat was that bad. And I was put on a beta blocker to help control my heart rate. But a lot of times even going from reclining to sitting up or sitting to standing would shoot my heart rate up.

I wasn't really able to do daily activities, cleaning my pets' litter, cooking, even showering and exposure to heat or high temperatures was extremely exhausting and I would just have to sleep for hours. Over time, the beta blocker has been helpful. I was on it for about six months and recently got off it because I was starting to see some recovery. So I stopped the beta blocker in January, started to feel fairly normal, and then my husband broke his wrist a few weeks ago, and just the compounded stress of having to take care of him and a relapse in my pets' health has caused a complete relapse for me. So I feel like I'm back at stage one, but potentially worse.

So there are some things that are better. The chest tightness is now better, but now any kind of emotional or physical stress, and by physical stress, I mean cooking a meal can count as physical stress. So walking downstairs to get my mail counts as physical stress, will bring all the symptoms back. So I've had, in the last couple of weeks, actually several emergency room visits, a couple 9-1-1 paramedic calls, because my heart rate will be so high that I feel like I'm going to pass out.

My tests have all come back normal. I've had several images and blood work and things. So it's really an enigma as to what might be going on. But the persistent heart issues are still very much a reality after what I thought was improvement over the past few months. So I'm really happy to be able to be here and share my experiences, hear from others that might be going through similar things. And again, thank you to FDA and team and collaborators for putting this together.

MS. BENT: Thank you so much, Sudeepti. We really appreciate your sharing this. There's a lot to unpack with everyone's experiences. And we need to thank Jill and Heather-Elizabeth, Linda, Estefania, Katie and Sudeepti for sharing. And they did this really to help us move the field of long COVID forward. So thank all of you.

So let me maybe turn briefly to my FDA colleagues to see if they have any clarifying questions for any of our panelists and to see if they have any thoughts on what they've heard.

Yes, please. Rear Admiral Iademarco?

DR. IADEMARCO: Yes. Thank you. It was really, really good to hear those presentations, and I'm sure it was very difficult to put them in terse terms. This was touched upon, but I wouldn't mind hearing from one or two of the panelist speakers/patients to describe a little more about the interaction with navigating the healthcare system, and especially the interaction between primary care and, if necessary, specialty care.

MS. BENT: Sure. So let me maybe turn to -- we'll go to Katie and then Heather-Elizabeth, and then Linda, and I'll just ask if you could keep your comments as brief as possible because we do want to also be able to turn to people on the phone. But when I say brief, I do not mean fast. So please go ahead and speak slowly so that we can interpret it appropriately. Thank you.

MS. DRACKERT: Absolutely. Thank you. And thank you for that question. So my situation with navigating the healthcare system required a lot of waiting. So I will say I'm lucky enough to have pretty good health insurance and a long-term relationship with a primary care provider. But even with that access, I still had to wait three months to get into a long COVID clinic, and I had to wait months to see certain specialists. Just a lot, a lot of hurrying and then waiting was my experience. And most of the time, I would say about half the time I was believed, and then half of the time I would be a little put down or dismissed because I'm young, I'm 28, and yeah, that's a little bit about my experience.

MS. BENT: All right. Thank you, Katie. Heather-Elizabeth?

MS. BROWN: Hello. Thank you. I would say that I have had a very interesting experience with the healthcare system since my experience. I have been fortunate that I do have a very comprehensive health plan through my employer. So a lot of the medications that I've had over the past three years, some of them have been upwards of $1,000 to $2,000 per refill that my insurance has covered for the most part. And additionally, a lot of the specialists and providers that I have found have been through my initial hospitalization and treatment for COVID, which I think has eliminated a lot of the issues that many people have had with being gaslighted, with gaslighting, with medical professionals, with issues with not being believed or having their symptoms overlooked because a lot of the providers that I worked with were the same ones who saw me in the hospital when I was first there, who got me through the initial hospitalization or were able to bring me through the coma or some of the other things that I've dealt with.

But I will definitely say that it has still been challenging. I similarly had to wait a long time to be admitted to the long COVID clinic here in Michigan. My waive was eight or nine months, and so it was quite a long time before I was able to be seen and then actually scheduling those appointments. So it has been an exercise in patience and faith. However, I do find that learning and having information about being your own advocate as a patient has been invaluable. And that's something that I have gotten more information from with a lot of the long COVID support groups and other organizations that I've been able to participate with. And I think that that's something that needs to continue to be addressed and presented to long COVID sufferers who need to advocate for themselves when it comes to getting proper health or medical care and connecting with providers who are going to help them move in the right direction in terms of recovery. Thank you.

MS. BENT: Thank you. And Linda?

MS. VARNO: Yes. Thank you. Great question. I want to highlight that when my son started having symptoms of pediatric long COVID, long COVID wasn't even terminology used. So initially, when we were seeking care out for Aidan and his anomaly of symptoms that were occurring, my husband and I were actually abused -- or excuse me, were actually accused of abusing our child or sexually abusing our child. And so that's how we were presented with happenings initially. So we were moving from healthcare system to healthcare system because no one was believing us, no one would listen to our son and they were looking at it from a psychiatric breakdown.

So initially our options in April to May of '21 were to put our beautiful, healthy prior to all of this 12-year-old son into a skilled nursing facility, to place him in a pediatric psychiatric unit or to look at pain programs which weren't comprehensive enough to really meet all the needs Aidan was seeking.

So for nine months we went without any provider helping us to really hone in on all of Aidan's problems and get us to where we needed to be because even our own wonderful, amazing pediatrician who has been with Aidan since day one just kept saying we need to get to specialists. Who are they? Where are they? So, for us, highlighting what Heather said, familial advocacy and also starting crowdsourcing through our Facebook page is really what led us to getting quality, amazing care at Rainbow Babies and Children's Hospital. So, thank you.

LARGE-GROUP FACILITATED DISCUSSION ON TOPIC 1

MS. BENT: Thank you, Linda. Really, really appreciate you. And so sorry to hear about Aidan's experience. So now we are going to take a few calls. We're going to start with Christine on line one. So let me see if we can do that. Christine, can you hear us?

CHRISTINE: Yes. Yes, I can. Can you hear me? Hello?

MS. BENT: I'm not sure that we have any sound from the phone. So we'll just give it a minute to see if we have any sound from the phone.

CHRISTINE: Can you hear me now? Can you hear me now? Can you hear me now?

MS. BENT: Yes. Yes, we can. Thank you.

CHRISTINE: Oh, great. Can you still hear me? Okay.

MS. BENT: Yes.

CHRISTINE: Great. Hi, everyone. Before my COVID infections in 2020, which were mild, acute infections, I had a very full life. I was 35 years old, working the job of my dreams in international development. I traveled the world frequently. I had a robust social life and was a devoted daughter. I loved dancing and skiing.

Since my COVID infections, I am no longer able to work any job, even part-time. I am primarily housebound and frequently unable to do activities of daily living, like changing my clothes. The ability to shower is rare for me. I am unable to communicate with family and friends without significant physical and cognitive repercussions. When I try to do too much, such as stay on a phone call too long or do house chores, I become mostly bedbound for a day to a week. I've gone for months feeling disoriented, as if my brain is inaccessible to me only because I used my brain too much over the course of one or two days.

I struggle with over 30 long COVID symptoms.

My diagnosed post-COVID conditions are ME/CFS, neurocognitive disorder, POTS, MCAS, small fiber neuropathy and CIDP. The symptoms that have had the most significant effect on my life are cognitive impairment and debilitating fatigue; more specifically, the worsening of these symptoms following any kind of physical or cognitive exertion.

In almost three years, I have not stopped seeking treatments that might help. I am fortunate to see several specialists regularly, including, but not limited to an ME/CFS specialist, neurologist, allergists and immunologists, psychiatrists, gastroenterologists and physical therapists for my neck pain. I often see additional specialists for second opinions. I follow several sources that report on potential long COVID treatments. I stay in touch with a large international group of friends with long COVID with whom I discuss which treatments we are trying and what is and isn't working.

A successful treatment would enable me to exert physically and mentally without worsening my ability level and sickness symptoms. It is imperative that decision-makers at the FDA understand that drugs that simply boost fatigue or cognitive function -- sorry, boost energy or cognitive function on any given day are not a solution and can even be harmful. Whenever I try a drug that improves my energy levels or my cognitive function, I exert more than I would otherwise physically or cognitively. And within a week, I end up in a much worse state that cannot be helped by medication, typically bedbound without enough energy to grab things from my nightstand and disoriented and unable to stay on a specific thought for five seconds.

Instead, we need treatments that prevent post-exertional symptom exacerbation. It is critical that the FDA takes this into account when reviewing clinical trial design. Thank you for your time.

MS. BENT: Thank you, Christine. Really appreciate you taking the time to share your thoughts with us. Let me now turn to Shawnee on line two.

SHAWNEE: Hello?

MS. BENT: Hello. So I can't hear Shawnee or the interpreters, but once I can, I will just ask people to remember to speak slowly so that the interpreters are able to interpret. So Shawnee, if you can, go ahead. Okay. So we're going to go ahead and try to get Shawnee back. Let me turn maybe now to Shannon to see if we have any comments that we want to share at this point in time.

Shannon, are we ready to share some of those comments or should we move on to polling?

MS. SPARKLIN: Yes. I have some comments that I can share.

MS. BENT: Great.

MS. SPARKLIN: A lot of the comments that we've been receiving have been stating that they resonate with what the patient panelists shared earlier during the panel. Regarding some of the major symptoms, I am seeing comments related to blood pressure issues, tingling and pain, light-heartedness, dizziness, brain fog and onset dizziness, eye redness, pain and blurry vision. One panelist -- or one written comment said that it feels like they're walking on a boat when they're walking and that they experience severe headaches, chronic insomnia, sore throats, rashes and that they experience difficulty standing and only laying down had helped their symptoms with that.

So overall, a lot of the comments are reflective of what we have heard so far. But I will continue to monitor the comments to see what else we receive.

MS. BENT: Thanks, Shannon. So let's now move on to just to some polling questions. As we mentioned previously, polling is still limited to participants who have lived experiences with long COVID, either as somebody with long COVID or as family members or loved ones. And so we will now move on to that. And so the first question that we have is how long or after your COVID-19 illness did you begin having symptoms of long COVID? And so please select the motion: A, 0 to 1 month; B, 1 to 2 months; C, 2 to 3 months; D, 3 to 6 months; E, 6 to 12 months; F, 12 to 24 months; or G, 24 to 26 months or other.

Okay. It looks like we're seeing a majority of people who felt like their symptoms really started to appear within that first month after their COVID-19. But it does look like we're seeing kind of representation from across the across the options with one to two months and two to three months being kind of the more common. So thank you. That's helpful information.

Let's move on to our next polling question. Which of these symptoms have you experienced because of your long COVID? Please select all that apply: A, pain, including headaches; B, learning, attention or memory difficulty, for example, brain fog; C, weakness or fatigue; D, shortness of breath or cough; E, racing heartbeat, dizziness, postural tachycardia syndrome, also known as POTS; F, post-exertional malaise or exercise intolerance; G, depression and/or anxiety; H, difficulty falling asleep or staying asleep, such as insomnia; and I, other.

All right. So it looks like we're seeing a range of symptoms and kind of a combination of symptoms across the board and so with really the attention and the weakness and fatigue being currently top but obviously significant impact from the racing heartbeat, the post exertional malaise, the insomnia and others as well.

Okay. So now we're going to move on to the next question. Now this next question has the same options as the last question, but in this question we're asking you to select the top three answers about which symptoms of your long COVID are most bothersome to you. And so you can select three. And again, those answers are, A, pain; B, learning, attention or memory difficulty; C, weakness or fatigue; D, shortness of breath or cough; E, racing heartbeat, dizziness, postural tachycardia syndrome; F, post-exertional malaise or exercise intolerance; G, depression and/or anxiety; H, difficulty falling asleep or staying asleep; or I, other.

And I will have to admit it's a little difficult for me to see the answers. But I think we're seeing that the weakness or fatigue, the post-exertional malaise and the attention -- difficulty with attention such as brain fog are really coming in as the things that people find the most bothersome with pain also being a significant factor and the racing heart rate or POTS. So we're really seeing that all of these are having a significant impact on the people who are answering the questions for this polling. So thank you for providing us with that information.

And then let's turn to our final polling question before we turn back to our callers on the phone. And so this is the final question. What do you find to be the most disruptive aspects of long COVID on your daily life? And again, please choose up to three answers: A, lost productivity, such as not being able to work as much as you want or being able to attend school to the extent that you need to; B, loss of physical function; C, loss of job; D, impacts on relationships with family and friends; E, emotional or psychological impacts; F, cognitive effects such as thinking and remembering; G, other; and H, none of the above. And I'm sure that this question is kind of difficult because it's really hard to pick the top three for things like this, right? But we appreciate just the fact that you're willing to kind of think about this and share your thoughts with us about this.

So we're seeing it looks like the cognitive effects are a significant impact. Lost productivity is significant. The loss of physical function is significant. Obviously, the impact on relationships with family and friends is also really significant to people. And so thank you for sharing this.

And we're now going to turn kind of back to the phones. And so let us turn to Robert on line six to share some of his experiences with long COVID.

Robert?

ROBERT: Can you hear me?

MS. BENT: Yes.

ROBERT: I'm a long COVID caretaker, and what we'd like you to know, my fiancée and I, is that my fiancée says she feels like she's disappearing. A year ago, we could walk one mile together, and a few weeks ago, we couldn't make it to the mailbox. She sits upright for less than 30 minutes per day and stands for less than 10 minutes, never consecutively. Sometimes she doesn't have enough energy to speak. Doing a crossword puzzle together this past Sunday began to deplete her. We can't go to a friend's birthday party, a wedding or even walk the dog to the park one block from our home.

We are missing from public life, and what's happening to her is happening to me. Because of her sleep issues, I now sleep on the sofa every night, and I'm just hoping that it'll help her sleep better and heal more if I'm in a different room. And then in the morning, I wake up and I make breakfast and lunch for her, and I put it on the table outside the bedroom as quietly as I can so that she can get up and walk as few feet as she needs to eat and hydrate herself. And then I go to work, and then I come home and I do the same thing for dinner and we have a few precious hours every day where we can run the risk of talking and enjoying each other's company without depleting her. So long COVID has transformed our lives completely and we desperately need help.

MS. BENT: Thank you, Robert. I'm so sorry that you're going through this and thank you for taking the time to call in and share your experiences with us.

Let me now turn to Shawnee on line two.

Shawnee? Hi, Shawnee. Can you hear us?

SHAWNEE: Can you hear me now?

MS. BENT: Yes. Please go ahead. I don't hear any speaking.

SHAWNEE: Hello? Okay. My name is (indiscernible). I experienced long COVID, but I am also epidemiologist working with the symptoms and this condition. In my personal experience, I moved from Puerto Rico to work with COVID-19 in East Texas in October 2020. I got sick with COVID-19 in January 2021 and I had to leave my job and come back to Puerto Rico because I was not able to do my daily living activities by myself. I fell related with chronic fatigue syndrome. I could barely stand to take a shower or walk short distance. I developed dysautonomia, like an orthostatic pressure problem. I experienced dizziness, palpitations or irregular heart rate, and I also experience detrimental lung function. I expand more than six months receiving respiratory therapy like three times per day. I had to buy a portable respiratory therapy machine.

I've suffered from asthma since I was child. But after COVID, I had new triggers for my asthma and I could have an asthma attack any moment. I also developed depression, anxiety and post-traumatic disorder. I had visited family medicine, to pulmonologist, to cardiologist and endocrinologist. Because my blood sugar was high. I started to receive medicine to control my blood sugar level. However, the doctors claimed that I was young and the other results of the test were normal. So I was supposed to be fine, even I didn't feel well. So basically the only doctor who treat me instantly was a pulmonologist (indiscernible). They gave me treatment to stabilize my asthma, although they say by the time that they didn't know the cause of those post-COVID symptoms.

So I basically had to conduct my own research to know what kind of recovery measures I can apply to myself. So I didn't receive physical therapy or referral to a rehabilitation program. I do had to visit a psychologist for the anxiety and depression because it was hard to know that I was not the same person I was before COVID. So I spent two months unemployed because I was not able to work. I had to regret accepting a job offer with benefits as an infection control coordinator in Florida. And then after two months of that, I started to work in Puerto Rico as well as an infection control coordinator. But I didn't feel well enough yet to drive or to walk. I had to do it because I was economically compromised.

So when I started to work, I noticed that I couldn't do the rounds in the hospital with the same ability that I used to. I had to take breaks in the middle of my shift and get some rest in my car and then go back to work. I also experienced brain fog, but fortunately I got a position as a disease intervention specialist developing a surveillance system for long

COVID in Puerto Rico which required less physical effort, but my brain fog made my performance difficult.

MS. BENT: Thank you.

SHAWNEE: I had a problem interacting with colleagues and it's something that I am still working with it.

MS. BENT: Thanks, Shawnee. That really is great of you to call in, and I apologize for the audio issues that we had kind of to begin with. But thank you for hearing your experience. It seems like it's had a huge impact on your life. So thank you.

So now let me turn to John on line seven. John, I'm wondering if, once we get you on the line, if you could maybe think about answering a question or two for me, if you'd be willing.

JOHN: Sure. What's the question?

MS. BENT: Thanks. Yes. So are there any specific activities that are important to you that you can't do or do as fully as you'd like because of your long COVID?

JOHN: Absolutely, and I think the activities are the ones that would help my family. I used to cook all the dinners, I used to clean up downstairs, I used to take the kids to the park and I can't do any of that physical stuff anymore. And I really have a lot of sort of internalized shame around not being able to provide for my family by working and doing those tasks anymore.

MS. BENT: Thank you. Is there anything else that you wanted to -- I know I kind of took you off of what you called to talk about. So is there anything else that you wanted to talk about related to your long COVID that you'd like to share briefly with us?

JOHN: Sure. I can do it real briefly. Yeah. I'm young. I was vaccinated. I had a really mild illness or acute illness and I just never got better. I've got a family with two young kids, used to be very athletic and used to run and ski, work full-time. And after COVID, I just -- something wasn't right. I was weaker. My heart rate started spiking. Contacted the doctor, they had no idea how to treat this. They said, just don't worry about it, and then just declined from there and realized I have really bad post-exertional malaise.

And that's just the important thing. I want to echo some of the other speakers is that the post-exertional malaise is the most limiting symptom. I could deal with the fatigue. I could deal with everything else. I could push through it and get what I needed to get done. But because I have that payback with the post-exertional malaise, I have to really limit my activities. So if there's some sort of treatment around lowering that or letting our bodies recover, I think that's the most important thing for the FDA to hear.

MS. BENT: Thank you. Thank you. Really appreciate that. Let me turn to Anne Marie on line ten.

ANNE MARIE: Hello?

MS. BENT: Hi, Anne Marie. I'd like to hear about your experiences, and it sounds like the experiences of maybe your child with long COVID. Also, I think if you wouldn't mind talking to us a little bit about whether your long COVID has changed over time from its original diagnosis to now, that would be great for us to hear about. And once again, just a broad request to speak slowly so that the interpretation is accurate.

ANNE MARIE: Sure.

MS. BENT: Thank you so much.

ANNE MARIE: Like many of you, I'm no longer afraid of the acute COVID illness. But I've learned the hard way that the story doesn't end when the initial symptoms subside. At the end of March 2022, three of the six of us in our house contracted COVID for the first time. We were all fully vaccinated and boosted. Despite being young and healthy, my 14-year-old son Luke and I never fully recovered after our infection. Luke initially improved slightly, but after overdoing it at a Scout event in May, he went into a huge crash that he has still not recovered from. He is now only doing school virtually from either bed or the couch.

While I had been substitute teaching, I now struggle to take care of my basic needs or do an occasional chore. We are shells of the people we were before COVID and lead a very limited life now. For the first few months, I just waited and expected we'd get better. But eventually I realized I needed to start researching, and I haven't stopped learning ever since. We've seen dozens of doctors, both locally in New York City and Philadelphia. We've had blood work, x-rays, MRIs, CAT scans, ultrasounds, physical therapy, myofascial release therapy, chiropractic and acupuncture with the hopes that someone is going to be able to help.

But the truth is there is no cure and no one is an expert because long COVID is still too new. There are only things to help minimize the symptoms to help us function a little better. In addition to the cost for all of this, which isn't all covered by insurance, the energy to figure out what to try, where to go and then actually attend all these appointments is truly exhausting. I've been diagnosed with dyssomnia, cough and mild emphysema despite never having smoked. And I'm exploring hypermobility, connective tissue diseases, ME/CFS, craniocervical instabilities. So the work is not done.

We both spend about 90 percent of our day laying down. We are not able to have our legs down or our heads up for any period of time. Our biggest issue is debilitating fatigue, fatigue that makes me struggle to hold my arm up long enough to brush my teeth or wash my hair. It's debating if I should just deal with the pain from laying in one position for too long because the idea of getting enough energy to roll over is unbearable. It's watching my once active teenager crawl up the stairs to get to bed.

The second most challenging symptom is post-exertional malaise, or PEM. Even if we think we have the energy to do simple tasks, we run the risk of having PEM afterwards. It can take several days after any kind of physical, mental or emotional energy for it to catch up with us, making our 20-plus symptoms flare.

Because of these symptoms, our family has missed out a lot over the last year. We had to cancel our family vacation to Disney last summer. We have no idea if or when we'll be able to reschedule, as we don't even have the ability to be upright long enough to have dinner at a restaurant, let alone take a big trip like that.

MS. BENT: So thank you for sharing that.

ANNE MARIE: I'm sorry. I have more to add, if possible.

MS. BENT: Sure. We do have just about 10 minutes left before we go to break, and we do have a few other callers on the phone. But if you want to finish up, that would be -- that would be -- go ahead.

ANNE MARIE: Sure. (indiscernible) real quick. There's a fine line between maintaining hope that we'll be cured and learning how to live with a chronic illness. Our physical therapist has been critical in teaching us ways to improve our quality of life. I cried leaving our first appointment because it was the first time I felt like someone understood what was going on. We've been taught that if we overdo it, we could risk creating a long-term setback like what happened with Luke.

The biggest thing we've learned is the need to rest (indiscernible). I basically have 10 to 15 minutes of being upright before I start to have problems. I have a handicap placard for my car so I can limit my walking, a shower chair, compression socks if we know we're going to have our legs down for more than a few minutes. I use noise-canceling earplugs and Luke wears sunglasses for overwhelmingly heightened sensitivity. I've learned how to feel better doing nothing. I'm not yet able to feel better when I do much of anything. While most of the world has moved on, COVID isn't over for my family. Even the healthy members of our family still take precautions out in public in order to avoid getting infected, and either, A, getting long COVID themselves since there seems to be anecdotal evidence of a genetic connection, or, B, getting me and Luke sick again and risk losing whatever progress we've made.

MS. BENT: Thank you. Let's turn now to Sawyer on line three. Hi, Sawyer. Thank you for calling in to share your experiences with us. Okay. Moving on -- hello? Okay, We'll move on to Tina on line four.

TINA: Hi. Thank you.

MS. BENT: Hi, Tina. I know that you might have some things that you want to talk to us about, and we'd very much like to hear them, but I'd also really appreciate it if maybe you could touch on whether your long COVID has changed at all from its original diagnosis.

TINA: Sure, no problem. So I got sick in July of 2020, and I will say that the first year and a half, about 18 months, was the hardest. I was severe at that point, possibly very severe. Now I'm moderate, so it has improved a bit, not from any specific treatment so much as managing my post-exertional malaise with strict pacing. Also, I call it giving up everything you love. So not walking, not trying to hike. I had to stop working completely. I couldn't even manage working from home.

Previously, right before COVID, I had backpacked the Appalachian Trail, part of it, and I volunteered for six different organizations. I worked full-time as a project manager. I played ukulele and sang. All of those things had to be given up. I'm now diagnosed with long COVID, POTS and ME/CFS.

I just wanted to add that it really has stolen almost the entirety of my life. I had to give up my house and move in with my parents as well. I now use a wheelchair to leave my house, to go shopping, and I have a shower chair and other aides at home. I just don't have an ability to be upright, to cook, to shower upright, to walk, to socialize with friends or work in any capacity without creating post exertional malaise. To echo someone else, I can take stimulants to get through the fatigue on a certain day. But I experience a crash for anywhere from four hours to a month. Last summer, I was bedbound for a month. So I just wanted to add that this really has stolen my life away. So I appreciate you holding this meeting and listening. Thank you.

MS. BENT: Sorry about that. So let's turn to the final call that we're going to be able to take before moving to the break. I'm going to turn to Kailin on line five to hear about some of your experiences. So, Kailin, if you wouldn't mind just briefly giving us a little bit about your experiences.

KAILIN: Yeah. Can you hear me?

MS. BENT: Yes, we can. Thank you.

KAILIN: Okay, great. Thank you so much for letting me speak. I think my experience probably echoes a lot of people's here. I was 30 years old, extremely active, no preexisting conditions, and I went from doing 40-mile backpacking trips to about a month after getting a COVID infection in June 2022 to basically being in bed 18 to 20 hours a day.

Like so many people who have spoken here, I was diagnosed with POTS, postural orthostatic tachycardia syndrome, myalgic encephalomyelitis or chronic fatigue syndrome, and small fiber neuropathy. And I'd like to emphasize that these are all lifelong chronic illnesses with no known cure and there's very little treatment. So I think in looking at treatments with about half or more of people with long COVID experiencing these other post-viral illnesses, it's really important to look at the treatments and research that's already out there with some of these post-viral illnesses.

These illnesses lead to a whole large constellation of symptoms, like a lot of people have spoken. I have probably over about 30 symptoms once I list them all out. And I would say in terms of progression, in the first four to five months of my illness, these were extremely limiting. I was working full-time as a journalist and a videographer, and I was completely unable to work for about nine months. I, like I said, was in bed about 18 to 20 hours a day, and lying down was the only thing that made me feel any sort of any better.

I have everything from tachycardia, numbness and tingling, to extreme heat and cold intolerance, extreme fatigue, exercise intolerance, and a big thing people have been talking about a lot, post-exertional malaise, which I'd like to emphasize is a little different from exercise intolerance. Sometimes I can do an activity in the moment or exercise in the moment, but then hours or a day or two days later, I'm left with a severe flare-up of my symptoms.

The cognitive piece is also absolutely huge one. I often find myself messing up words, unable to find words, unable to write or swapping in different words when I write, which is hard as a journalist and often feel like I'm thinking through mud. And those kind of post-exertional malaise crashes can be pretty severe.

I've had people describe it to me, and this sums up my experience pretty well as like a conscious coma, like the world is going by around you. You can hear everything, you can see what's going on, but you can't move or speak or even really form thoughts. And it's extremely disabling.

I have gotten a bit better, and the only way that I have gotten better is with medications to deal with POTS as well as just honestly extreme rest. Like I said, being unable to work and just trying not to exert myself as much as possible and practicing pacing, periods of rest and exertion have helped. So I've gotten a bit better, but I would not say I'm recovered. I'm still nowhere near the person that I used to be.

MS. BENT: Thank you. That is helpful and I appreciate you kind of speaking to the little bit of improvement. I'm glad there's some. I certainly wish that there was more for you and for everyone that we're hearing from today. So right before we head to break, and I know we're at time, but I'm going to turn to Shannon just to give us a brief summary of the comments that we received through the Web.

So go ahead, Shannon.

MS. SPARKLIN: Thank you, Robyn. We're seeing several comments regarding flare-ups of symptoms and symptoms that are random and unpredictable. I've also seen several comments regarding exercise intolerance or energy crashes related to post-exertional malaise.

Many people in the comments described how they used to be very active and now they're unable to exercise. They have energy crashes throughout the day, and they're exhausted from simple activities.

I'm going to read a few comments that we received regarding the impact of the symptoms of long COVID on daily life. One individual stated that they're not able to prepare their own meals, they eat cereal and milk twice a day, they cannot clean, they're single and live alone without family help and no financial resources to pay for the things that they need.

Another commenter wrote in that they have had long COVID for over nine months. Prior to getting acute COVID and long COVID, they would bike 25 miles twice a week and they were enjoying their best life. Now they state that they cannot walk slowly for more than 30 minutes without getting post-exertional malaise the lasts two to five days, which results in total fatigue.

Another commenter discussed their reduced work availability and schedule and difficulties with being self-employed and how their income has been reduced dramatically as a result of their long COVID symptoms.

Another comment stated that I was a very active mom who practiced yoga and ran half marathons before I tested positive for COVID in April 2020. Three years later, I still struggle with fatigue, severe brain fog, migraines and the effects of POTS, which includes heart palpitations, increased heart rate and painful blood pooling upon standing. I have extreme issues with ADLs such as showering and cooking. ADL stands for activities of daily living. She stated that they're a military family with their primary care doctor on base and that continuity of care has been an issue as physicians change bases often.

So those are just a few of the comments that we have received. Thank you.

MS. BENT: Thanks, Shannon. So now we're going to go to break. I apologize to those of you who were on the phone who we weren't able to get to. Once again, I do want to give a quick plug for the docket comments. I think we've barely scratched the surface today as far as the daily impacts of what you are all experiencing on a daily basis. So please consider sharing your comments to the public docket to expand upon what you've shared so far. We're now going to break for about 27 minutes and we'll be back to reconvene at 12:45 Eastern Time. So thank you all and thank you to our panelists and our callers who really got this meeting off to a great start, and I look forward to seeing you all back in just a few minutes. Thank you.

(Recess)

TOPIC 2: CURRENT APPROACHES TO TREATMENT

MS. BENT: Welcome back, everyone. I hope you had a great break. We have a limited time, so we're going to move straight into topic two. As we mentioned before, topic two will focus on current approaches to treatment for long COVID, your experiences and your perspectives on that, what you're currently doing to treat your long COVID, and whether you feel like your long COVID is well managed and finally, what are you looking for in a treatment for long COVID.

We have five panelists who will start off our discussion by sharing their experiences. And before we launch into our panelists' experiences, I just want to let you know that our first question for the open discussion session is what are you currently doing to treat or manage your long COVID, how has your treatment regimen changed over time and why and what symptoms would you like most to be improved or resolved by treatment.

So now, as I mentioned, we're about 30 minutes away from people calling in to share their answers. And now I'd like to welcome our session two panelists and thank them for joining us today. I'd like to start by inviting Stephanie to share her experiences with long COVID.

Stephanie, if you want to, go ahead.

MS. HUGHES: Sure. Thank you.

MS. BENT: Thanks.

MS. HUGHES: Thank you, Robyn. My name is Stephanie Mitchell Hughes. I am from Columbus, Ohio, and I've had long COVID since February of 2021. My treatment for long COVID consists of being a patient at the post-COVID recovery program that was established by the Ohio State University Wexner Medical Center in response to COVID-19 patients who were returning with symptoms that some of which were not -- were very different from what they experienced with the COVID-19.

And as a patient in the clinic, I received a checkup initially across all of the major systems within my body, including my lungs and my cardiac system, and my long COVID affected from a physical perspective my pulmonary system. And so I was sent to and became part of the pulmonary rehabilitation department. And I also at the same time became part of the physical medicine department because I received treatment in the physical medicine department for brain fog.

And with respect to the pulmonary rehab department, in July of 2021, I started pulmonary rehab. I completed 24 sessions of pulmonary rehab by October of 2021. The pulmonary rehab consisted of two sessions twice a week on Tuesdays and Thursdays. And initially we did an initial walking exercise just so that they could gauge where we were.

I had a smaller group of people who -- two to three other people who were in my group who were also patients in the post-COVID recovery program. And we also were constantly monitored by two to three rehabilitation -- I'm sorry, respiratory therapists. Our first exercise was the treadmill. As I am still told, it is the most important machine that we used. And we also used a bike. There was a bike that we used and they have bikes of different levels that you can use when you were doing the bike exercise. We also did and worked on something called an arm ergometer. And then we did some free weights and some standing and sitting exercises.

The goal was not so much to increase necessarily speed, but rather capacity and the length of time that we were able to do a particular exercise or work on a particular machine, and we were always encouraged to work at our own pace.

One of the other things that they did was we were also weighed. At the beginning of each week, we were weighed to see if we were losing weight. And there were also a few classes that we could call in and listen to if we wanted.

I decided after the 24 sessions of pulmonary rehab, and there are 24 sessions because that's the number that my then health insurance paid for. And I decided to continue on with pulmonary maintenance. And I typically go to pulmonary maintenance on Tuesdays and Thursdays in the early afternoon. And in pulmonary maintenance, I work alone. I don't have -- well, the respiratory therapists and other people in pulmonary rehabilitation are there if we need to ask questions, if I have questions or something like that. But I do pulmonary maintenance alone. Unlike with pulmonary rehab, I don't have a respiratory therapist asking me how hard I'm working or measuring my respiration or something like that. And so that's the one thing that I continue to do consistently.

I also initially when I was working with someone from physical medicine on brain fog, there were a number of -- what they were trying were a number of different medications that would treat symptoms. So, for example, one of the medications that I took was an old Parkinson's drug called, and I figured out the name, amantadine and really didn't like that very much. And so I decided to stop taking it. And I just continue if I need to call in for support. There are a number of different healthcare practitioners who I have in the program, and I can call any of them for support at any time. So my primary person is the person who I call my long COVID internist.

MS. BENT: Thank you. That's great input. It's wonderful to hear that you've been able to kind of get plugged into care, and hopefully it's really having a great impact. So thank you for that.

So I am going to move on to Jackie right now. But thank you so much, Stephanie, for sharing that. Thanks. Jackie, let me turn to you. Are you ready to share your experiences?

MS. LUCIANO: Yes. Can you hear me okay?

MS. BENT: Yes, I can. Thank you.

MS. LUCIANO: Great. All right. Thank you, Robyn, for the introduction and to the FDA for inviting me to be here to share my perspective. I'm a current long hauler since January 2022 and have complex associated conditions such as dysautonomia, POTS and suspected myalgic encephalomyelitis. I had to put my career on hold as a regulatory nurse consultant. I suffer daily from several symptoms of long COVID, and finding treatment for these symptoms has been an insurmountable challenge.

I've been bounced around over a dozen specialists and was often refused treatment because they were either not FDA approved for long COVID, blood work was normal or there are not enough studies. Initially, I was prescribed daily exercise, and I learned the hard way that this caused harm, and I've been suffering the consequences since then. Thanks to advocacy groups such as MEAction and Long COVID Justice, I learned what post-exertional malaise is and tips on how to stop, rest and pace, which I must continue to do every day because, yes, exercise still causes me harm now.

By October 2022, I couldn't complete rehab due to the post-exertional malaise, and I was still being prescribed more medications despite taking over 30 pills a day, and kept having adverse effects. During an ER visit for an acute flare, I was appalled that I was treated inhumanely by healthcare staff, and I'm disgusted by how the medical system is still failing patients. Thanks to a wonderful online community who have shared their experiences with complex conditions, I have learned about and tried various interventions, noting that what has worked for others may or may not work for me and vice versa.

Partnering with providers who believe me, who keep up with the latest research and who help me prioritize treatments for viral clearance, sleep, dysautonomia, hormonal balance and staying within my energy envelope have allowed me to better manage my symptoms and activate my body's innate ability to heal. Examples include vagus nerve stimulation, neurobiofeedback, mitochondria and neuroimmune infection control supplements. I started avoiding dairy and gluten to decrease inflammation and reintroduce massages, acupuncture and chiropractic care to help with lymphatic drainage, circulation and pain management.

I also have to pay for IV hydration and electrolyte replacement at private clinics to prevent ER visits. I weaned off of several prescribed medications because I was either getting more side effects or I no longer needed them. But I do continue on hormone replacement therapy, antihistamines, midodrine and supplements. There's been a lot of trial and error, and thankfully I am currently sleeping better and have improved blood flow. But I still experience fluctuating disabling symptoms. Thus, all of the above are still not enough.

We need an operation warp speed for diagnostics and treatments for long COVID and associated conditions. Treatments need to address inflammation, viral persistence and reactivation, immune system dysregulation, hypoperfusion, mast cells, hormonal imbalances, menstrual cycles, microclots, cognitive gut, autonomic dysfunction and more. Each person is unique; therefore, treatment plans must be individualized and in addition to addressing the root physiological causes of symptoms, the overall goals must be to safely improve one's functional baseline and quality of life as many of us are still grieving our former selves.

I'm grateful to have access to a range of providers, but I wish care was accessible and affordable to all who need it. The best resources and information are from the patient community, who generously use their scant energy for the benefit of others. The information we need has not been available by government agencies nor the medical establishment, and I was one of those nurses, but not anymore. In collaboration with fellow long haulers and allies, we started a global toolkit to help empower patients and caregivers to provide hope and to remind everyone not to give up. Stay tuned. Thank you so much for recognizing us patients with lived experiences as experts and how post-infection associated conditions can no longer be ignored. Together, we will make a difference. Thank you.

MS. BENT: Thank you, Jackie. Really, really appreciate you sharing your experiences. Let me turn now to Daniel. Daniel, if you want to go ahead and share your experiences, we would very much appreciate it.

MR. LEWIS: Thank you, Robyn. When long COVID has taken everything from you, your money, your job and career, and all your goals in life, when long COVID has taken your appetite, your sleep, your breath, your comfort in your own body, your ability to stand or move, your balance and your memories, when it's taken your whole life outside your home, your sense of belonging, your dreams for the future, your independence, your dignity, your security and your freedom, all you have left is hope that research into treatments will deliver you from immiseration and your unthinkable fear that you will never get better.

We need safe treatment options now. Three years have passed. Over a billion dollars has been spent on research without producing a single approved treatment. Hundreds of billions of dollars have been spent on healthcare and hundreds of billions more on lost productivity, lost wages and disability.

We have experienced unfathomable suffering and loss. We do not have three more years. We will not survive three more years. I have seen countless doctors and taken over a dozen different medications, but they are all for symptom management or they're ridiculous long shots, nothing that we expected to heal me and none of them has fundamentally improved my condition. And nothing can manage my most disabling symptoms related to exertion.

I take a beta blocker and midodrine for POTS and Bupropion for fatigue. They are the only things I have found that help at all. And they only help a tiny bit. I am missing work and I can't access disability benefits. I am missing weddings and bat mitzvahs and holidays. I am missing time with my family, friends and community. I am missing my chance to get married and start a family. I have lost over ten pounds and my muscle mass is depleted. I am literally wasting away.

This is a matter of life and death for many, and for the rest of us, it is a matter of life and a life so circumscribed by disability and pain that it's hardly a life at all.

We need safe treatment options now. Trial ambitious new treatments that modify this disease and give us a fighting chance at recovery. Launch new clinical trials today. We are waiting for our chance to try sulodexide, Ampligen, Inspiritol, temelimab, ibudilast, BC 007, RSLV-132 and many other drugs still in development. Use crossover trials, expanded access, emergency use authorization, accelerated approval, fast track all the tools at your disposal to get these potentially lifesaving treatments to patients.

And while we wait for novel treatments we need to be able to try antivirals for COVID, antivirals for reactivated viruses, JAK/STAT inhibitors, anticoagulants and antiplatelets, metformin, combination maraviroc and pravastatin, and all the other drugs that already have FDA approval and have shown promise in early research but are still hard to get.

Both primary care physicians and specialists don't know what to do with us. Doctors need clear and direct clinical guidance to prescribe these potentially lifesaving treatments to patients.

This illness is defined by loss, and we are losing everything, even our memories and our sense of who we are. We are hanging on by a thread. That thread is the hope that things will change, that the NIH will fund clinical trials for ambitious long COVID treatments, that researchers will understand long COVID's disease process and how to interrupt it, that drug manufacturers will recognize that if the U.S. has already spent over half a trillion dollars on medical expenses related to long COVID, then we'd be willing to spend a hell of a lot more than that on a treatment that works, that the FDA will authorize promising long COVID treatments without delay, that clinicians will treat their patients with compassion and urgency, administering treatments ethically and equitably, that patients will have the treatments they need to live and that we will be so successful that we can use America's response to long COVID as a model for how the world should treat all patients with debilitating chronic illnesses. Thank you.

MS. BENT: Thank you, Daniel. Let us now turn to Tammy to hear some of your experiences. Tammy?

MS. WILSHIRE: Hi. Good afternoon. My name is Tammy Wilshire. I became a COVID long hauler as a result of a March 2020 initial infection. My experience, especially in regards to seeking treatment options, is a long and very complex story.

I think it is important to mention that I am a resident of a small rural farming and coal mining community in the west central Appalachian Mountains of Pennsylvania. Due to this, my access to care was and still is very limited; therefore, my biggest challenge to receiving proper treatment.

Early in the pandemic, we did not have access to COVID testing here. As a result, I found that a presumptive positive test did not allow me to take advantage of a lot of the care clinics and treatments that later became available. My treatment is a continually evolving plan. We put out the major fires such as cardiac issues and endocrine issues, while ignoring the other more minor fires, such as neurological issues and pain management. I had to deal with most of these things myself, with some help from my caring but overwhelmed primary care physician.

Even when I was hospitalized with cardiac issues in July of 2020, I heard frequently it must be anxiety, and I was not taken seriously. It took me almost 18 months to begin to find help, mostly through specialty doctors over two hours away, and through long COVID groups online. To date, I have tried physical therapy, supplements like vitamin C, D3, B12 and magnesium, beta blockers for my tachycardia, gabapentin and other neuro meds for the tremors and the worsening fibromyalgia, statins for increased cholesterol and vascular inflammation from COVID, pain creams, muscle relaxers, anti-nausea and GERD medications and more with just limited success.

Of these treatments, I initially had the most success with physical therapy. I saw an improvement in my stamina/strength and in my POTS heart rate. However, after about two weeks, as we added more exercises, I began to feel a lot worse. My ME/CFS relapsed with crippling fatigue. After PT, I would find myself needing to rest. Eventually, I was bedbound again for a day or two following the session due to the post-exertional malaise, and I had to discontinue physical therapy due to exercise intolerance.

Due to new endocrine and GI issues, I've had to change my diet to a low carb and anti-inflammatory plan. I have to make time to eat every three hours in order to keep my blood sugar stable. This requires quite a lot of effort and planning while balancing my energy levels, and it still isn't completely solving these issues for me.

I would 100 percent say that my long COVID is not well-managed at this time. After three years and two probable COVID infections, I am just now being examined by specialists for issues that started in 2020. The dynamics of my symptom presentation have definitely changed. Some things have gotten better on their own or with some medical management, but I still suffer with quite a lot of symptoms that are not well-controlled for various reasons.

I fully suspect that there will be no one size fits all cure for long COVID. Each individual is unique in their presentations and their symptoms. However, just an improvement in pain relief and fatigue would be amazing. Thank you for allowing me to share a small part of my long COVID journey with you today.

MS. BENT: Thank you, Tammy. Thank you for sharing that with us. And for our final panelist, we're going to hear from Angela.

Angela, if you want to go ahead.

MS. VAZQUEZ: Great. Thank you so much. And thank you to the FDA for hosting this important forum on long COVID. My name is Angela M. Vazquez and I am president of Body Politic, a grassroots health justice organization and home to one of the first global COVID-19 patient support groups.

Before getting COVID here in Los Angeles in

March 2020, I was a runner for nearly two decades. What started as a mild illness progressed over weeks with an increasingly scary set of symptoms including severe blood clots, a series of mini strokes, brain swelling, seizures, painful heart palpitations, severe shortness of breath, extreme confusion and numbness in my face, hands and legs that progressed to an inability to walk for several days and new onset of anaphylaxis. All of these were largely untreated and not even acknowledged by physicians for nearly a year.

So the first thing I would like to emphasize is that long COVID patients from the first and second waves of the pandemic had a fundamentally different trajectory than those who came after us. Just because we weren't hospitalized does not mean we shouldn't have been. In fact, we experienced severe but unaddressed symptoms in 2020 and also come from communities of color, represent some of the sickest and most medically marginalized patients that deserve urgent specific treatment and prioritized access to clinical trials.

With long COVID, I now have several chronic conditions, including ME/CFS. My most debilitating symptom is known as post-exertional malaise, but which I experience as post-exertion neuroimmune dysregulation. My PEM is composed of my worst symptoms like insomnia, cognitive dysfunction and confusion, sleep apnea, heart palpitations, fevers and chills, severe migraines, joint and muscle pain, invisible tremors and muscle jerks. I have developed a strict pacing regimen that allows me to work from home full-time but not do much else.

My long COVID conditions (indiscernible) others come out to play in short order. I take 15 different medications regularly, many several times a day, and most to manage my mast cell activation and autoimmune inflammation. I also get weekly four hour Benadryl and saline infusions. I'm on a number of expensive supplements to support my mitochondrial health, and I also now have severe joint and nerve pain in my neck and face, and an MRI has shown marked disc degeneration in my neck.

My doctors suspect that long COVID triggered inflammatory arthritis in my cervical spine and could be driving many of my neuroimmune symptoms, something I've learned is not uncommon for patients like me with inherited or acquired connective tissue disorders. I am currently exploring regenerative medicine options for my neck, as physical therapy has only been marginally effective. None of these treatments address the core drivers of my long COVID.

One of the biggest ongoing barriers to getting treatment is the lack of providers knowledgeable about infection-associated chronic conditions who can make accurate clinical diagnoses and develop a coherent treatment plan.

I highly recommend clinical trials not base their cohorts exclusively on diagnosis-based conditions, but also include symptom clusters that reflect the evolving knowledge of these conditions, so those who lack access to knowledgeable providers, especially low income people of color, are not excluded from treatment trials.

Finally, I was also recently reinfected and I was lucky enough to get an extended course of Paxlovid for 15 days per the clinical trials for long COVID. My conditions flared quite extensively for several weeks and my post-exertion malaise is now much more prominent. I highly recommend clinical trials build in protocols to manage worsening of symptoms, especially when treating chronic infections. For example, chronic Lyme disease patients (indiscernible) regarding what is (indiscernible) to antibiotic treatment. Despite an extended flare, Paxlovid seems to have prevented a significant (indiscernible) in my cognitive dysfunction and also seems to have eased my gastrointestinal issues. The gut-brain axis of mutually reinforcing inflammation appears key for me. I was also one of the few who improved after my first vaccine. So I am very interested in how treating persistent or reactivated infections could impact my long COVID.

So I'll close with saying that my request to treatment developers (indiscernible) please focus on this thing called post-exertion malaise. While each person's malaise may look different, it follows a unique and distinct pattern across patients who have it. We need to know how it relates to mast cell activation and blood clots, orthostatic intolerance and blood flow to the brain and nervous system, how persistent infections exhaust the immune system and erode connective tissue surrounding the spinal cord. The answers are there. We just have to look at the body much more globally than we ever (indiscernible).

MS. BENT: Thank you, Angela. So, once again, those are some really compelling and diverse experiences, and I want to thank all of our panelists, Stephanie, Jackie, Daniel, Tammy and Angela for sharing their experiences.

So at this point, maybe let me turn to my colleagues, FDA and HHS colleagues, to see if we have any clarifying questions for the panelists before we turn to some of the callers that we have. So colleagues, I don't know if you have any questions. If not, maybe we can turn back to you after we take a few calls from the callers. All right. I don't see that we have any clarifying questions, which I think is a testament to how clearly everybody was able to share their experiences.

So let me then turn to our callers online. Let me start with Sawyer on line one.

LARGE-GROUP FACILITATED DISCUSSION ON TOPIC 2

SAWYER: Hello. Can you hear me?

MS. BENT: Yes, I can. And before you get started, there's a little bit of a challenge for our interpreters with the phone clarity. So if you would be willing to just speak slowly and clearly to help optimize our chances of successful interpretation, I'd really appreciate that.

MR. BLATZ: Yeah, definitely.

MS. BENT: Thank you.

MR. BLATZ: Yeah. So I'm Sawyer Blatz. I was a previously healthy and extremely active 26 year old. Long COVID has been devastating and life ruining for me since my first mild infection in November of 2022. I eat a healthy diet, worked out five times a week, was recently boosted and had no preexisting conditions. I have lost my work, my ability to leave the house, my ability to run and weightlift and even simple things like being able to shower daily or cook meals for myself. It's safe to say that in my current state, my long COVID is not well-managed, despite lots of attempted interventions.

My worst symptoms are crushing fatigue, POTS, cognitive dysfunction and insomnia. These symptoms have resulted in me being almost entirely bedbound and my partner being my full-time caretaker. All of my symptoms are worsened by exertion and can lead to crashes. On my worst days, suicidal ideation is constant, and the immense grief I've experienced from the full life I can no longer live is crushing.

My current treatment course is trying to address reactivated viruses like Epstein-Barr virus, which I tested positive for, with antivirals like valacyclovir. It's too early to say if this is helping me, as it could take months for it to have an effect. But it has shown promising results for some folks with ME/CFS.

We desperately need the FDA to help expedite research into treatments that solve the underlying pathology of long COVID, not just symptom management. And when promising interventions are found, we need them to be authorized with emergency approval. Treatments specifically looking into post-exertional malaise and orthostatic intolerance like POTS are of intense interest to me. Myself and millions of others have lost our lives to this disease. Please take our suffering seriously. Thank you for your time.

MS. BENT: Thank you, Sawyer. Let me now turn to, let me see, Maria on line five.

MARIA: Hi. Yes.

MS. BENT: Thanks. Go ahead, Maria, if you want to talk to us a little bit about what you're currently doing to treat or manage your long COVID, and if that regimen has changed over time at all, that would also be really helpful for us to know.

MARIA: Yeah, absolutely. I am a formerly healthy 31-year-old woman with long COVID from my first infection. Currently, my routine includes prioritizing rest, avoiding inflammation and taking a variety of supplements and sort of natural herbal teas and foods to either treat my symptoms or attempt to address the root cause of my long COVID based on hypotheses I or other patients have developed. I avoid exercise, stress and situations where I might be reinfected to the detriment of my social life and my career.

I manage my long COVID decently well, but constantly fear that I will deteriorate and will not be able to recover. Unlike many of my peers and my medical providers, I am well-aware of the risks of long COVID. I've had multiple doctors tell me that my fatigue and my inappropriately high heart rate are the result of deconditioning, despite having been an athlete for my entire life, had a cardiologist tell me that I should not exercise, and then later revised that to say that I should. She would not prescribe me any medications and did not have other suggestions on how to address my vascular symptoms.

At this point, every day I eat fermented foods like natto and take nattokinase and serrapeptase supplements, which I learned about online. There's a strong community of long COVID patients, and I've learned more there than from any single doctor. Those supplements are known for their abilities to break down fibrin and proteins and blood clots. This markedly improved my energy and helped against fatigue, but seemed to have an upper limit of effectiveness. I informed my cardiologist about this and the supplement's anticoagulation qualities, not the other way around, as it should have been.

I'm self-treating on the assumption that I have microclots and inflammation in my vascular system and possibly a lingering infection. But without medical supervision, I know I need to be cautious about other risks. I have read that triple anticoagulant therapies are fruitful for some patients, but working alone, I can't risk causing other health problems by thinning my blood too much. I have no medical team with which to pursue a more aggressive therapy, and as I never had a positive PCR test, I can't get into long COVID clinics or clinical trials.

I prioritize rest, which my doctors have not even recommended, but I know from other long COVID patients that can be crucial to recovery. In addition to the first supplements I mentioned, I take coenzyme Q10, a variety of B vitamins, vitamin C, magnesium and vitamin D, which I was already taking as I've been deficient in the past.

My PCP ran many blood tests at my request, which turned up abnormalities like elevated lipids, including triglycerides and cholesterol, which has always been on the low side for me, but offered me no follow-up care or explanation for those abnormalities or concern for these new unhealthy markers. I was already aware that these are possible results of a COVID infection, though I don't know the mechanism for this metabolic change or how to reverse it when I already have a clean diet and cannot exercise.

My primary care provider did not even remark on this change in my health or suggest rudimentary improvement. I was also screened for autoimmune markers but received no feedback on these results. Again, after listening to other patients, I'm working to reduce inflammation in my body in the hope that my symptoms are partially caused by a positive feedback loop that I might (indiscernible) out of. What if that inflammation is serving some important purpose, like fighting a lingering infection? I don't have anyone to guide me, and I worry that I will prolong my recovery by trying the wrong tactic.

I also have test results suggesting viral persistence of herpes viruses, but my PCP has not connected those to my current status. I'm weighing the risk of reinfection via additional visits to a facility with no mask mandates in order to suggest antiviral medications. As I've read online and we've heard from other callers, that that has helped other patients, but I feel as though I'm the one piloting my care when acclaimed medical facilities in a major city should have experts to guide me.

I've also read about stellate ganglion blocks and existing treatment to reset dysfunction in the autonomic nervous system. Many of my symptoms, like inappropriately high heart rate and breathing issues point towards this system as the root of my problems, but no doctor has given me any assistance on how to modulate my nervous system or improve my health there. I could pursue a stellate ganglion block on my own time and through a private practice, but I might just be scammed, or I might come up with worse health in the end. Many patients report success with this off-label application of the procedure, but there's little research on whether it's an appropriate treatment, whether it's a risk or a waste.

I'm frustrated that I keep coming up with series of hypothetical treatment plans for myself instead of getting personalized, effective care from trained professionals. I've also read about the potential of the Novavax vaccine to succeed where mRNA vaccines have begun to fail, but I cannot access it. I only hear about its potential from the long COVID community, not medical outreach or PSAs aimed at vulnerable populations.

With my current long COVID, I'm scared that an additional mRNA booster might lead to an increase in symptoms, as some patients report, though others do see improvements. It feels like a roll of the dice, and for a vaccine that's less protective against each new variant anyway. I would like to see Novavax as an option for vaccination. And if I'm taking my healthcare decisions into my own hands, I would at least like to be able to act on the research that I read. I have read a variety of hypotheses.

MS. BENT: Thank you. Thank you, Maria. I'm going to ask you maybe to just focus on maybe one or more two more quick, quick points, because we do need to move on to other callers as well.

MARIA: Sure.

MS. BENT: Please go ahead. Thank you.

MARIA: In general, I'm an intelligent and highly educated person, and I'm comfortable weeding out pseudoscience and misinformation, and I'm open to advice from outside the medical system. But as many patient research projects and hypotheses are proving correct, from the existence of long COVID itself to mechanisms like microclots in the blood and viral persistence, we are exhausting ourselves spending so much time, effort and money in search of cures that could be more efficiently found, tested and publicized by major medical establishments.

I hope some of the topics that I mentioned here will be picked up and fast-tracked, as they seem to have potential. But as a study of one, no patient should have to be testing theory after theory on themselves in hopes of leading a healthy life. Thank you.

MS. BENT: Thank you. Let me turn to Christine on line ten.

CHRISTINE: Great.

MS. BENT: Hi, Christine. I know you're a little bit faint, so is there any way we can -- let's see.

CHRISTINE: Oh, is it any better?

MS. BENT: Yes, that is much better.

CHRISTINE: Okay. Okay.

MS. BENT: All right, please --

CHRISTINE: Please let me know if it fades out again.

MS. BENT: Okay. I will do. And I know we have a good number of people on the line, so I'm going to ask you to maybe just keep your comments to two or three minutes. Thank you so much.

CHRISTINE: Absolutely. Yeah. I was asked to comment. I'll be commenting on my treatments and then the symptoms that I'd like to see prioritized. So I first had COVID in November of 2020 prior to vaccinations. I've had long COVID for two years, since March of '21. It started at the moment I had my second

COVID vaccine. I had an anaphylactic reaction to the Pfizer vaccine, and then that -- all the antibodies mixing fired off, everything I deal with now. So my therapies treat, Band-Aid, suppress or help me cope with my long COVID. I have not reached a point of an optimized functional life. Part of my treatment includes prescription, over-the-counter medications and supplements. I use methylphenidate, which is Ritalin and naltrexone, and those are both off label for long COVID, which means we pay out of pocket for those.

The methylphenidate was prescribed for POTS, but that Ritalin actually helps my brain fog and mental clarity much more. The naltrexone is for inflammation, and that is very helpful. I receive saline infusions twice a week for my POTS diagnosis. That is very helpful. It gives me much more focus and energy on infusion days. The saline increases my plasma so the blood moves more independently, kind of like a lava lamp through my body.

I have participated in occupational therapy. The purpose of that was for energy conservation. I got connected with TheraSpecs prescription, fluorescent, UV and blue light filtering glasses, which are a godsend for the light intolerance. I have participated in speech therapy for the brain fog, word recall, memory.

It's given me permission to tell people I need a pause. These therapists didn't have a long COVID protocol, so they used traumatic brain injury and stroke protocols, which I responded to.

I did pulmonary therapy, but I was not able to reach the goals because of exercise intolerance. I made it through about eight sessions. I was doing 16 sessions on a recumbent -- or 16 minutes on a recumbent bike. I went to 18 minutes. At the end of that 18-minute session at a very, very low exertion rate, I stood up and had intense bout of syncope. So I have not completed pulmonary therapy.

When I am more stable, I will do vestibular therapy and physical therapies for balance, stability, coordination and strength. I wear a digital medical ID bracelet because when I have my syncope episodes, I also have seizure-like activity and I'm unresponsive for 15 to 90 minutes. So that bracelet has a QR code on it, and anyone with a phone can access my important information when I can't speak for myself.

I'll start counseling services next week because the reality of living with this, as everyone has said, is devastating, and it's very likely that I will not be able to return to elementary teaching next school year. I use a Fitbit to monitor my heart rate with my

POTS. I use meditation as a form of mental and physical relaxation. If I can walk a little bit outside, I do, or I just sit outside. I've started using noise-canceling earbuds for sound sensitivity so that I can participate in life a little bit. So those are my treatment plans.

The particular symptoms of long COVID that I prioritize for treatment are my intense nervous system issues, which include syncope with seizure-like activity that happens several times a month and then presyncope symptoms, nerve damage, vertigo, fatigue, hyperhistamine reactions, the brain fog and neuropathic POTS. So that's all of my information. Thank you for listening to me.

MS. BENT: Thank you, Christine. Really appreciate you calling in and sharing that and really speaking to the specific question that I asked, so I really appreciate that. Thanks. So we're going to take one more call right now, and then we're going to move on to some polling questions. Let me turn to Carly on line 11.

CARLY: Hi, can you hear me?

MS. BENT: Hi, Carly. Yes, I can hear you.

CARLY: I'm going to try to make this as brief as possible.

MS. BENT: Thank you. Brief, but speaking slowly, right?

CARLY: That's right. I have all the POTS, ME/CFS, chronic fatigue stuff that you have heard over and over again. I was initially infected in October of 2020, and my first long COVID complication resulted in hospitalization in January of 2021, approximately eight to nine weeks later. I was admitted to ICU with exceptionally unstable vital signs and I was treated for migraines, and I believe it was coded as a migraine admission. I had a history of chronic migraines prior to my COVID infection and was undergoing many treatments for that, but it was well-controlled.

The summer before I contracted COVID, I was on a boat every weekend, staring at glares on the water, rocking back and forth, drinking cocktails. None of that is possible now. In addition to hospitalization, every year I participate in physical therapy, occupational therapy and home health services to rehab myself back to my disabled baseline after hospitalization. I have annual surgical ablations to treat migraines. Additionally, I take many medications for migraines. I'm not going to list them all. Lots of medications, lots of dietary supplements.

Some of these treatments have caused elevated liver function tests and I've had to stop them. I take so much Zofran, it gives me serotonin syndrome. Seriously, I'm a zombie because I take Zofran. It's ridiculous. My POTS and heart failure with preserved ejection fraction that was diagnosed by double right heart catheterization is treated with metoprolol, spironolactone, Jardiance, 6,000 milligrams of sodium daily and electrolyte drinks.

I use a mobility aid, trekking poles for walking, and a shower chair with a handheld shower nozzle. I take three antidepressants for depression and sleep. Notably, on my last hospitalization, I was also suicidal due to the fact that I was so terribly sick. As soon as they treated my electrolyte imbalance, the suicidal ideation went away.

I am to begin pulmonary rehab in June, as I have just last week completed my first appointment with a long COVID provider. I have moderate lung disease and I'm going to start the pulmonary rehab and the Dulera. I also take medicine for tremors. I would not say my COVID is well-managed because my POTS symptoms and my migraine symptoms keep me parked on the couch. I don't go outside. I don't go on dates. I don't go out to eat. I don't go visit my friends. So no, being shut in is not well-managed.

Prior to COVID, I was a 43-year-old, very active hiker, paddle boarder, bicyclist, even did a sprint triathlon at one point in the not too long past history, and now I am completely unable to exercise. The things I would look for in an ideal treatment would be treatment for brain fog, fatigue and temperature intolerance. Those are my most limiting symptoms that impair my ability to even pursue hobbies. Thank you so much for giving me the time to share my story.

MS. BENT: And thank you, Carly, for sharing your story. We really appreciate that. So we are going to turn back to callers in a few minutes, but first we're going to move on to some polling questions to get feedback from all of you who are joining us online. Polling does remain limited to participants who have lived experiences with long COVID, either personal experiences or as family members and loved ones. And so now we're going to move on to questions for topic two.

The first question is currently there are no medical products approved for treatment of long COVID. However, some treatments have been used off label. Which of the following medical products, that includes drug therapies or medical devices or interventions, have you used to treat the symptoms of your long COVID? Please check all that apply. And this includes --

sorry, apologies. Answers are, A, antidepressants; B, sleep aids; C, antivirals; D, antihistamines; F, analgesics, pain medicines such as acetaminophen or NSAID, so Tylenol or Motrin or things like that; G, corticosteroids such as dexamethasone, prednisone or cortisone; H, medical devices or other procedures; and I, other.

So it looks like we're seeing a lot of use of all of the different categories that we listed here. We're seeing -- it's hard to tell. It looks like the antihistamines, the Benadryl or diphenhydramine are one that is largely used by the group, some medical devices, analgesics, pain medicines. So, yeah, it looks like there's a lot of use of all of these categories of medicines across the board.

Is it possible for us to go back and show people the QR code one more time? I feel like maybe we didn't show that recently, so our participants for session two might not have necessarily access to that. Okay. Great. So it's being shown on the screen in the video feed, so you all should be able to see the QR code there if you need that to access the poll. Thank you.

All right. Let's move on to our next question. Which of the following interventions have you ever used to manage the symptoms related to your long

COVID? Please check all that apply: A, pulmonary rehabilitation or aerobic exercises; B, vitamins, herbal supplements or dietary supplements; C, diet modifications; D, meditation; E, acupuncture; F, physical or occupational therapy or rehabilitation; G, psychological or cognitive behavioral therapy; H, other; or I, none of the above.

All right. And looking at this, we're seeing a good number of people have been using both meditation and dietary modifications, as well as vitamins, herbal supplements and dietary supplements. We see a number of people who have been able to take advantage of physical or occupational therapy or rehabilitation. All right. And a good number of people, 12 percent of people who are saying other. And so that's also helpful for us to know.

Maybe while we're waiting for these results to come in, I can turn to Shannon to see do we have any themes about treatment options or any comments that you've been receiving related to treatment options, Shannon?

MS. SPARKLIN: Yes. Thank you, Robyn. We've received several written comments related to treatment options, many of which are reflective of what the panelists shared earlier. But just to list a few, there's a wide range of prescription medications, over-the-counter medications, as well as other therapy options that commenters have used. Just to list a few, they've listed ibuprofen, Trazodone, Lexapro, riboflavin, prednisone, antibiotics, low-dose naltrexone, low-dose Abilify, Novavax, Amplogen, beta blockers. And then in terms of alternative therapies, commenters have mentioned acupuncture, enhanced external counterpulsation or EECP therapy. They've also discussed nutritional supplements, ginger, physical therapy, rest and pacing, and vitamins and other supplements.

And overall, another theme that I'm seeing in the written comments is regarding a difficulty with accessing medication and treatment options due to doctors or physicians not believing their symptoms or not knowing how to treat them or lack of diagnosis. Thank you.

MS. BENT: Thanks, Shannon. Really, really appreciate that. And so looking at the responses from both the prior question and the current question, I think we can see that a lot of people have tried a lot of different treatments.

And so I'm going to turn now back to some of our phone callers to see maybe if they can talk with us a little bit about any medications that they've tried. What aspects of long COVID do their medications address well, and what aspects do they not address well? And so let me turn to Rebecca in Georgia or on line one to kind of share with us maybe her thoughts.

REBECCA: Hi, can you hear me?

MS. BENT: Hi. Yes, Rebecca. Is this Rebecca?

REBECCA: Yes.

MS. BENT: Yes, we can hear you. And so I was wondering if you would be willing to talk to us a little bit about the different types of treatments that you've tried, particularly medicines, if they've addressed any aspects of long COVID or maybe if there are any aspects that they do not address. And I would just ask you because we do have a number of people calling to keep your comments relatively brief, but also to speak slowly.

REBECCA: Okay. Well, just try to bear with me a little bit. I have some communication issues. I've had some strokes after COVID.

MS. BENT: Okay.

REBECCA: So bear with me a little bit because I do stutter a little bit and slur my words a little. So bear with me a little.

MS. BENT: That's fine. We're more than willing to bear with you. We appreciate you calling. So thank you.

REBECCA: Thank you. So I got COVID in February of 2020. I was a healthcare worker, and so I got it in February of 2020, and I first developed long COVID over spring of 2020. I guess by July, I was first hospitalized in October, and then by February of '21, I had my first stroke. Sorry, I'm trying to quickly get to my point here. Over the course of '21, I was hospitalized numerous times, and where it was found that I had multisystemic organ damage, my lungs, my gastrointestinal system, my gallbladder. I had lung damage, brain damage. So I had different areas. I had developed cardiac conditions. I had no cardiac conditions prior, no pulmonary conditions prior to COVID. I developed asthma, post-viral-induced asthma. I am now on six inhaler treatments and four breathing treatments a day from my asthma that I got from COVID. I now have to take two different blood pressure. I have stage three hypertension from COVID. I have significant amount of brain damage. I have damage to my frontal lobe, my basal ganglia and my right parietal lobe. I have lesions throughout my brain and my brain stem. And I have also developed four brain aneurysms, which are inoperable unfortunately.

Unfortunately, the majority of this is because of my cardiac conditions that developed from COVID and then not being treated, going unchecked because I tried to get into long COVID clinics, and even after being listed as a long COVID patient, I couldn't find a long COVID clinic in my area that would accept me. I couldn't get -- even now, even though I'm listed as a long COVID patient on all of my -- I'm diagnosed as a long COVID patient, and it's on all of my charts. I'm not being treated anywhere as a long COVID patient.

I'm seeing over a dozen different specialists, but at no point am I being treated as a long COVID patient. I'm not getting any long COVID specific treatments. I'm being treated only for the different types of damages that I have sustained from long COVID, from my pulmonary system, my cardiac system and gastrointestinal system. Everything that I'm getting is only damage specific. Nothing is actually long COVID specific. And that's part of the problem. Long COVID damage has gone unchecked, and it's pretty much I'm only receiving treatment for the damage after it's happened. There hasn't been any treatment happening as it's gone along, even though it's been recognized that what's happening to my body has been as a result of COVID infection.

And this has been three years of this happening, and it being recognized by doctors that this is all the result of multiple infections now. And sorry, losing train of thought. And I've now received a potential terminal diagnosis because my brain aneurysms are inoperable and I have clots surrounding them. So my doctors have told me that I could die at any moment, and surgeries probably won't save me if my brain aneurysms do rupture.

MS. BENT: That has to be incredibly terrifying. I'm so sorry.

REBECCA: Yes. I'm sorry. We desperately need research and treatment for people. I'm sorry. I get very emotional, but we need research for people and treatment because this is me three years into this, and I am day 20 of my fourth infection right now. This is what's going to happen to people if COVID goes unchecked and people don't get the treatments that they need.

I'm dying right now because I have not gotten treatment, and this is what's going to happen to millions of people. I am severely disabled. I have severe brain damage. I am bedbound and have to have other people take care of me. I have beginning stages of dementia. I'm 45 years old and can't take care of myself.

MS. BENT: Thank you, Rebecca. I really am sorry that you're experiencing this, but I really do appreciate you calling in and kind of sharing this with us because it's important information for us to hear. Let me now turn to Kevin on line three.

KEVIN: Thank you very much.

MS. BENT: Hi, Kevin.

KEVIN: Yeah, thank you very much for having this session with the FDA. I think it's great. It's wonderful to hear so many people calling in and getting those perspectives. I hope you do more of these calls in the future. I'm not going to go into my experiences with long haul COVID. I'm just going to go into treatment.

MS. BENT: Thank you.

KEVIN: Luckily, I'm blessed. My wife is a physical therapist, so I've got that at home. Acupuncture is another key thing for people to look at for helping with some of these symptoms. But the biggest thing I think anyone should be able to do is find a functional medicine doctor. A lot of the Western medicine took a look at the blood test and they could see problems. They just didn't know how to fix them.

I had elevated liver enzymes. I was diagnosed with Hashimoto's thyroiditis, destruction of the thyroid and a number of other things. But it was the functional medicine doctor who actually looked through and got me onto supplements and vitamins. Two of the companies that are ideal are based here in the United States, Optimal Health Systems and Apex Energetics. Both of those companies have stuff, medicines or supplements that can help with reducing some of those post-exercise malaise as well as reducing fatigue. There are B vitamins that can help people. Those are a key thing.

The problem, I think, with some of the research that isn't being done is, let's look at these things. Let's look at, rather than try and do some sweeping thing that's going to fix everything, find out what's wrong with people and fix those particular things. So B vitamins can help people make it through the day, vitamin D, vitamin C, melatonin for people to help get through the night. These are key things. I still have the virus inside me. So there's a product, Optiviral, which helps to reduce that and get one healthier. There's Optimal Defense. All these things can help people recover and put those things into check. Some of the things like the Hashimoto's thyroiditis will never truly be fixed. But what I can do is put it into remission. So the key thing is we need more of that research into functional medicine. I think that's the key thing that we're missing.

MS. BENT: Thanks, Kevin. That's really helpful. Has your long COVID kind of changed over time? Has it been -- I mean, have you seen -- are you -- or did you -- yeah, let me just stop there.

KEVIN: So my long COVID was very debilitating. I had a number of symptoms. One of them included feeling like I had food poisoning every two weeks on the dot, and I would be sick from anywhere from a day to three days not being able to hold down anything. So it was putting some of those things in check and getting some of those liver enzymes. Western medicine doctors were like, all those supplements aren't going to help. A month later, they took a look and they're like, wow, you got your liver enzymes close to normal. It was ten times normal, and you've somehow reduced it in a month.

And so those are the key things we need to find functional medicine doctors. That's what we need to start looking at, is putting more research into that, because that was the only way I could put some of these things into check and start to get back to a regular functioning. Yes, there are still some times when if I exert myself way too much, I'll be exhausted. But it is not as bad, thanks to those vitamins and supplements. But they are expensive. So I do spend several hundred dollars every month on vitamins and supplements, but it's the only way to make it through my days right now.

MS. BENT: Thank you. Thank you so much. Let me now turn to Tom. Tom, are you on the line? Sorry. I didn't say -- Tom, on line two. Apologies.

TOM: Well, so thanks to the FDA for reaching out and listening to the patients. This is obviously a major, major issue in the U.S. and worldwide. Just real briefly, I am kind of in a unique position. I'm a scientist, background in cell biology, molecular biology. I got my PhD in immunology, yet I'm also a long hauler. And so I've been trying my very best to connect all the dots and try to figure out what's going on in my own body personally and with the other suffering long haulers. And I'm currently running -- I'm excited to be running a clinical trial called Diet and Fasting for Long COVID. It's a remote trial that people can participate in in the U.S. And it's basically they do their -- alter their diet and do periodic short water fast, and we monitor their overall long COVID symptoms.

MS. BENT: Thanks, Tom. I think it would be really helpful if we could hear kind of about the treatments that you've tried personally and your personal experiences.

TOM: Yes, I'll do that right now.

MS. BENT: Thank you.

TOM: So the way I stumbled upon this approach was I've been battling long COVID for three years, since early in the pandemic. And just by chance, initially, I was ravenously hungry and I gained like 15 pounds. And I don't like diets. I decided to restrict my time, my eating, to just eight hours per day. And I went to a low sugar, no wheat flour diet and after doing that for a couple of weeks, I remember the Sunday I had a major flare-up of my brain fog or headache, and then suddenly after that it was gone. And that was miraculous.

I live in Colorado. I was able to start doing half-day hikes in the mountains, although initially I had severe shortness of breath at altitude and I found that I had severe post-exertional malaise the next day. So I'd be fine for a half-day hike and then I would have the PEM would hit me the next day and I'd have to nap for a couple of hours.

I had been reading and on YouTube and everywhere kind of exploring the potential of this internal cellular house cleaning process called autophagy. And one thing that is known to stimulate this internal cellular house cleaning process are short water fasts. And so I tried my very first water fast. I did a three-day water fast where I didn't eat anything, although I did drink salt water for electrolytes. And then I rested for a couple of days and amazingly, I was able to do a full-day hike in the mountains. And the very next day I did a second big hike in the mountains. So all of a sudden my post-exertional malaise was gone. In fact, I was fortunate to fully recover after four months.

I got COVID again. After some elk hunting and backpacking. It was much more severe. And I started doing these periodic short one- or two-day water fasts, like once a week or once every other week. I also started taking like on the weekends, I wasn't doing a water fast, I would take 600 milligrams of resveratrol, another putative autophagy inducer, and that's mostly known from cell culture research because they can't yet measure this well in living and breathing people.

Anyway, I had 10 or 12 typical symptoms and by March I recovered to zero symptoms. Severe insomnia was my last symptom to suddenly go away and I had zero symptoms for a month. And then I had severe emotional stress related to my mom's suddenly declining health. And also I did some heavy spring snow shoveling in

Colorado, which was ill-advised, and a day or two later I had a relapse and I had symptoms I'd never had before. My stools turned white for a week. I've seen a kaleidoscope of symptoms and I think a long lot of long haulers do.

MS. BENT: Yeah.

TOM: And my hypothesis is that I very much fall in the low level viral persistence camp. I think our cells are sick, we have associated cellular metabolic dysfunction and I think that wherever we have the aches and pains, like our gut aches or our brain fog or random kidney pains or chest pains, I think that reflects sites of viral persistence. We can't prove that yet, but the Chair Tau, et al. NIH study certainly shows the virus is capable of infecting a wide variety of cell types and organs.

MS. BENT: Great. Thanks so much. Thanks so much, Tom. Really, really appreciate you calling in. I know you were on hold for quite some time, so really appreciate your patience with us as we moved through our callers.

TOM: Yeah. No problem.

MS. BENT: So now I'm going to turn to Beth on line seven.

BETH: Hi.

MS. BENT: Hi, Beth. Thanks so much for calling in and your willingness to kind of share your thoughts about some treatments and your treatment experiences.

BETH: Thank you. Yes, and I'll be brief. I know you're doing a great job sort of keeping us on track and I know we all have so much to say because there's not a lot of people out there listening to us. So I feel everyone's frustration and I honestly just want to thank everyone for how brave they are --

MS. BENT: Yes, absolutely.

BETH: -- who've called and be so transparent. And I could sort of repeat most of what everyone has said as far as symptoms and devastations to my life and my family and everything. But I'd like to address treatments because that's what we're speaking of now, or I feel like more lack thereof. I honestly think that the well-intended sort of mainstream approach to medicine that America has, has almost, certainly not on purpose, for most, I believe made it worse for many of us. And I think that really needs to be heard by those who have the power.

I have notes, so forgive me, and they really are short. But because of my memory, it's difficult for me to sort of stay on track. And I've tried to write down my thoughts during this because literally in doctor's appointments, I think what people don't realize is we forget what to talk about in the doctor's appointment. So when we finally have a doctor and we need things addressed, we forget them. And these clinics, these so-called clinics aren't set up like a cancer center. They aren't set up with patient advocacy. They aren't set up.

I liken it to sort of opening clinics that are for paraplegics, but not having ramps for them to get in, asking them to get up and walk over to get weighed. They're ill-equipped. They're not prepared for us. And three years into this and I got sick in June of 2020, to me, it's sort of disgraceful, honestly, because the damage that this is doing to us, the added damage, is insurmountable that in getting, trying to get treatment, even at the supposed best clinic. I moved up here temporarily from Florida to Washington DC to get help from what was a so-called clinic opening up at George Washington. Everybody in that hospital is gone by their own frustration.

So that's one issue that I think we can't ignore. Many doctors who I've had sort of off the record conversations with agree. Many have left the clinic, quote, unquote, because of their own frustrations, but I think the damage it creates in us, even listening to this call, and I'm sure many of the patients and long COVID people are experiencing what I'm experiencing, which is just this heightened level of sort of PTSD, which I struggle with a lot.

My main symptoms now, although there's a myriad of symptoms, are severe memory loss, PTSD, stuttering, bruising, POTS, huge executive function issues, heart shock, insomnia, muscle atrophy. But what's interesting to me is after months of expensive physical and cognitive therapies, from the, quote, unquote, best, from Mount Sinai to George Washington, basically everyone came to the conclusion that all this trial and error, which I understood and still understand, that I wasn't going to make much more improvement until I got a handle on my PTSD, which I agree with, by the way.

But there's sort of this block that happens. It's really difficult for us to physically and cognitively heal when you're suffering from this odd sort of unusual, not yourself anxiety or PTSD, for lack of other diagnosis. I don't know what it's called, but it's bizarre.

MS. BENT: And so is that what you're thinking, what you're thinking, that would be the symptom that you would prioritize for treatment, as it's kind of the gatekeeper to maybe some of the others in your case?

BETH: I do, I talked to a lot of people. I think most of us have learned more from each other than anywhere else. But one of the problems though is that, and it's almost a governmental problem, so it's great that we're talking to you guys, because when doctors can regularly hand out opioids and narcotics, but they can't hand us injections of vitamin D to take home or glutathione or B12 or all of these things that a lot of people have identified as help, there's something wrong with that system.

This gentleman, Kevin, talking about spending hundreds of dollars. I'm in that same boat and I can't afford it. I'm going bankrupt over it. The other thing that I found really interesting is so it seems like the very things that are helpful to us, like, for whatever reason, the government doesn't sort of get involved in, which is supplements and functional medicine, Eastern medicine approaches, and it's hurting us.

One thing I do want to ask for the doctors to look at is in physical therapy, I heard people talking about getting on treadmills, and here we go again, this fancy word, Pilates, that seems like it's something that rich housewives do was the most successful approach to my getting through some of my physical therapies because, think about it, you get to lay down, you can strengthen your body without being upright, but yet my insurance won't cover that. That's my --

MS. BENT: All right. So I'm just going to ask you just -- I think we need to wrap it up because we're running short on time, and there are others that -- and some polling questions that we need to get. So if you maybe want to choose one final topic.

BETH: Well, I think that's it. I would ask you guys to look at the things that you probably don't normally look at. And while you've been three years looking for answers, you have a lot of people giving you the same exact information. It's supplements, it's physical therapies that maybe aren't the norm that need to be looked at. And we need help to get them and get them immediately so that we can live our lives and become better. So that's what I would ask is that you would look where you don't typically look and help people financially get these things through the mainstream as opposed to them having to be self-financed by so many of us. Thank you so much.

MS. BENT: Thank you. So now we're going to take a brief break from calls and we're going to turn back to our final polling question for the session. I hope everyone has their cell phones ready and we'll be moving on to that question in just a moment. So for the question, the question is for the medical products or interventions that you use, what would you consider to be the most burdensome aspect of the treatment?

And you can choose up to three answers. The answers are, A, how the treatment is administered; B, the time it takes to receive or administer the treatment; C, the treatment only provides minimal benefit; D, the treatment is effective only for a short term; E, there are bothersome side effects of the treatment; C, you have a concern about serious risks from the treatment; D, there's uncertainty about the long term effects of the treatment; H, there's difficulty accessing the treatment; and I, anything else.

All right. And looking at the responses, it seems to be mostly split between difficulty accessing treatments and the treatment can only provide minimal benefit. But it seems like people are endorsing all of the responses.

All right. So maybe now, while we're looking at these results, let me turn to Shannon. Shannon, do you have any comments that you want to share about people's thoughts on ideal treatment and priorities?

MS. SPARKLIN: Yes. Thank you, Robyn. So in terms of the comments we're receiving regarding ideal treatments and symptoms that individuals with long COVID would prioritize for treatment, many comments are saying that patients would prioritize treatments that improve fatigue and post-exertional malaise and brain fog.

One comment regarding ideal treatment stated that an ideal treatment would include not just treating symptoms, but treating the root cause of issues. And that individual would want to look at the root cause, which includes drugs for mitochondrial dysfunction, IVIG for immune deficiency and autonomic dysfunction, and anticoagulants and vagus nerve stimulation for autonomic dysfunction and microclots. And that same individual would prioritize treatment for post-exertional malaise and general fatigue.

Another comment mentioned that a successful treatment outcome would be them being able to be more functional in their daily life, work full-time and get back to some of the physical activities, including hiking that they used to enjoy. Another comment mentioned that they would like for treatments to focus on microclots, viral persistence, managing symptoms while work continues to identify mechanisms and causes, and that managing the symptoms would be helpful to include careful screening for post-exertional malaise before recommending physical therapy or exercise, since that can tend to exacerbate the post-exertional malaise. Thank you.

MS. BENT: Thanks, Shannon. We only have about five or six minutes before break, so we're going to try and take maybe two more calls before we move into the read. Our questions are going to -- we'd really like the people calling in to speak a little bit about what we've just been talking about, the challenges to some of the treatments, as well as kind of what they would look for in an ideal treatment for long COVID.

And so with that, let me turn to Laura on line four.

LAURA: My problem with accessing treatment was that I was gaslighted and I was having severe shortness of breath, but they only gave me treatment for that because I was asthmatic. If I weren't, they would have just dismissed me. And I had to find my own treatments. And I had a severe fatigue and post-exertional malaise. I was too weak to feed myself, but I had to look into research myself on chronic fatigue and found that I could take CoQ10 soft gels and NAD or niacin and L-carnitine. And I regained my energy by leaps and bounds. And my pulmonary and other symptoms mostly went away too because my body had the energy to heal itself. But I had to figure that out myself. I also found compelling information with fresh ginger has improved my energy level even more, and I'm very energetic now, and it helped with brain fog and limiting sugar also helped me. But I had to be my own doctor.

And because of the gas lighting, there's a long COVID clinic in my town, but I don't feel I can go there because the doctor who gaslighted me was also there. And the gaslighting just accumulates in your medical file and it encourages other doctors to not take your symptoms seriously, which can be a very big problem, especially if you're in the EE with heart attack symptoms. But if I could get treatment from a doctor, I would like an antiviral. There's one not available in the U.S. So I can avoid reinfection and not get who knows what other symptoms that I may not be able to treat myself. Okay.

MS. BENT: Yes. Thank you very much.

LAURA: Okay.

MS. BENT: All right. Let me turn to Adina on line ten as our final caller to just share a little bit of experience before we read out to break. And Adina, I apologize, but we only have a few minutes before the break.

ADINA: I will keep it brief.

MS. BENT: Thank you.

ADINA: Thank you for taking my call. Thank you to the FDA for focusing on patient-focused drug development for long COVID. Prior to COVID, I was a healthy 40-year-old who was working three separate part-time jobs in the modern gig economy. I've lived in New York City for 20 years, and I do not drive, so I've always walked a lot. As a gig economy worker, I was used to walking one to two miles regularly to save money.

I've had long COVID since I was first infected in March 2020. My symptoms have included profound fatigue that makes it impossible to shower or even brush my teeth sometimes, PEM, which is post-exertional malaise, joint pain and swelling, limb pain, inappropriate sinus tachycardia, palpitations, lightheadedness, orthostatic intolerance, brain fog, numbness and burning pain in my left leg, dry eye and intermittent tinnitus, ear pain, throat pain and nausea.

The symptoms are worse if I do too much. Doing too much can make all of my symptoms worse. Too much can mean too many hours of sedentary, office-based work. It can mean showering and then getting dressed.

It can mean vacuuming the floor. I've been treated at the Mount Sinai Post-COVID Care Center since August 2020. I was referred to pulmonology, cardiology, physiatry, neuropsychology and more. Each of these specialties has treated me separately in turn and looked for anything diagnosable that can be pinned to an existing test.

The cardiologist diagnosed me with post-viral fatigue syndrome, post-viral dysautonomia and severe obstructive sleep apnea, as well as familial hypercholesterolemia, put me on statins and eventually beta blockers to address my inappropriate sinus tachycardia. The pulmonologist found a blood clot in my right lung in December 2020 and put me on an anticoagulant, which helped me with a sharp stabbing chest pain as well as with calf cramps and an inability to walk.

Cognitive neuropsychology said that I did not have brain damage but I had some issues, including poor fine motor control and variable processing speed, as well as poor phonemic fluency. As someone who used to copy edit complicated legalistic documents in multiple languages, I could have told them that I was having issues with phonemic fluency.

I was further referred to hematology and rheumatology. Rheumatology identified some abnormal autoantibodies but no diagnosable autoimmune condition. She recommended that I stay on top of monitoring some of these abnormal autoantibodies. Physiatry recommended electrolytes and maximum compression, high-waisted runner leggings.

Finally, I've been seeing an ME/CFS specialist since April 2020, when I was diagnosed with ME/CFS. She put me on a number of supplements that are meant to address mitochondrial dysfunction and eventually also low-dose naltrexone, which is an off label use. I don't know if any of the supplements are helping, but the low-dose Naltrexone helps with my joint and limb pain.

I did physical therapy first at Mount Sinai and then through the Pulmonary Wellness Foundation here in New York City. I think that the pulmonary wellness that included supplemental oxygen, both while I walked slowly on a treadmill and while I rested afterwards, helped me while I was doing it, but the effect disappeared once I stopped their protocol after a few months.

I have found some things for online patient support groups that have helped, including curcumin with black pepper extracts that seems to help my joint pain and swelling. Over time, with all the specialties I've seen and everything I've tried, I've seen the most improvement by resting, pacing and convalescing. Staying within my energy envelope does the most for keeping my symptoms tolerable.

The symptoms I would absolutely prioritize for treatment in my case are fatigue and myalgia. I desperately wish that I could walk miles without consequence again. I desperately wish that I could work a full-time job again. I've managed to increase my work from two to five hours a week during my first two years of long COVID to about 10 hours a week now. But I can't do 10 hours a week during weeks when I also do too many things such as any cleaning or socializing.

An earlier caller said that the interventions they've tried so far have been to treat, Band-Aid, suppress, help or cope. It's a very good line. I agree with that. I think that drug development has to focus on root underlying causes and addressing them rather than suppressing symptoms without addressing whatever is causing them. In addition, more treatments have to take a person's whole body into account. It's very hard when everything is subdivided into specialties and subspecialities.

Challenges to treatment are that they are expensive, not covered by insurance, such as supplements and low-dose naltrexone, which is not FDA approved for ME/CFS and so it's prescribed off label and that they don't work that well or they don't suppress all of the symptoms. Finally --

MS. BENT: And Tina, I'm sorry. we're running a little bit over. So if you could limit it to maybe just one more comment. Thank you.

TINA: My last point is that I know the FDA -- I know federal government agencies oversee supplements in the U.S. But someone should (indiscernible) to know what you're buying what the bottle is saying is inside. So many people are trying so many supplements to treat long COVID, and it really needs to be overseen by someone from the government. That's it. Thank you so much for your time.

MS. BENT: Thank you so much. Really, really appreciate and apologies that we have to move on to break now. So for now, we're going to move to a 10-minute break. We'll reconvene in 10 minutes, which I believe will be about 2:32 Eastern time, and at that time, we'll move on to topic three for the day, clinical trials. Thank you all, and we'll see you in just 10 minutes.

(Recess)

TOPIC 3: CLINICAL TRIALS

MS. BENT: Welcome back, everyone. I hope you had a good, albeit brief, break. In keeping with our theme for the day, we have limited time, so we're going to move straight into topic three. As we mentioned, topic three will focus on your thoughts around clinical trial participation. This includes sharing what you think about when considering whether or not to participate in clinical trials, what outcomes of trials for long COVID do you think are the most important things to measure and what experiences have made it easier or harder for you to participate in the clinical trial.

We have five panelists who will start off our discussion by sharing their thoughts and experiences. Before we launch into our patient experiences, I do want to let you know that our first question for the open discussion session is if you considered participating or have participated in a clinical trial for long COVID, can you please tell us about your experiences. And so with that, we're about 30 minutes away from people sharing their answers.

So now let me turn to our panelists and ask them to share some of their experiences with us. We're going to start off with Michelle. Michelle, would you please share some of your experiences with clinical trials and some of the things that you considered?

MICHELLE W.: Yes. I am a parent of four children, two of whom have long COVID. My daughter was 16 and a half when she got COVID in July of 2020. Her life has been totally changed since that infection. She was an honors student who was going to graduate high school at least a year early with a goal of becoming a doctor, but instead she is unable to start college. She has had multiple hospitalizations, abdominal surgery, used a feeding tube for 18 months, collected many diagnoses and now takes many, many medications that cost our insurance tens of thousands of dollars each month.

We used the study that was published by Mount Sinai about autonomic reconditioning therapy to guide her physical therapy treatments both in a clinic as well as incorporating physical therapy using equine movement to treat the physical fatigue and the worst of the physical symptoms. Currently, her most debilitating symptoms are significant cognitive changes, language issues, cognitive fatigue and daily headaches.

Professionally, I'm a physical therapist. As a healthcare practitioner, I am very aware of the need for research and clinical trials to determine underlying causes of disease and treatments for them. When I saw the NIH was funding a large study to determine the pathophysiology and treatments for long COVID, I knew my daughter and I needed to participate. The RECOVER trial has made it easy for us to participate. We are lucky to have a site only 20 minutes away from our home. Because I manage my children's healthcare needs, I now only work two days per week. Study visits are able to be scheduled on my days off. There are surveys that we complete at home. Staff at the study site have been easy to reach via email or phone. Results from standard lab tests are forwarded to us so we can submit them to our doctors to avoid duplicate testing.

Due to the timing of when my daughter was tested for COVID, she did not test positive. However, she had known exposure, lost her sense of taste and smell and is now clinically diagnosed with long COVID. The lack of a positive test did not interfere with her ability to participate in the RECOVER study, which is very important, especially for patients who were infected early on in the pandemic.

Currently, of the studies for long COVID that are listed on clinicaltrials.gov, very few do not require a positive PCR test. Therefore, she is not eligible to participate in the majority of studies. We recently chose to not participate in a study for one diagnosis that she has because it required stopping a very effective medication that took many months to find the correct dose for her. And she did start to participate in a different study of a computer-based cognitive rehab program. But unfortunately, she had to stop due to a significant increase in her symptoms due to the cognitive exertion required.

When we assess participating in a study, we look at does this study address one of her key impairments? What are the eligibility criteria? Will there be an opportunity for the control group to receive the study intervention? What are possible side effects of study interventions? Do treatment current medications need to be stopped? How many study visits are required? Is there a location close to where we live? Can study visits or activities be done virtually? Is there compensation for participating and are the risks of the treatment worth it?

Whether the treatment is a rehab protocol, medication, supplement or something else, our most meaningful outcome at this point would be finding a treatment for the cognitive dysfunction and cognitive fatigue that is preventing her from returning to her baseline function and from being able to go to school and move forward with her life.

MS. BENT: Thank you, Michelle. That was

really, really informative, and I think we'll probably want to kind of ask maybe some clarifying questions in a little bit.

Let me now turn to Ezra. Ezra, would you mind telling us a little bit about your experience as well as your thoughts when considering clinical trials?

MR. SPIER: Absolutely. Thank you so much. Hi, everybody. My name is Ezra. I live in Oakland, California, and I've had long COVID for seven months now. As a participant in a clinical trial, to me, it all really comes down to three things: impact, practicality and compassion. So I want to talk about each of those as relates to the study I'm currently in, which is a double blind trial of Paxlovid for treating long COVID.

So first, impact. Impact can be broad and it can be narrow. For me to be excited about a trial, it needs to have broad impact. I want to test a compelling and impactful hypothesis. In my case, it was a no brainer. Paxlovid is a great way to test the viral persistence theory, so there we go for big impact. But studies also have potential impacts on me, and those could be positive or negative. On the positive side, here is my chance to potentially get a drug that might actually help. Amazing. Again, no brainer. Even better, the study lent me a smartwatch and a blood pressure cuff for a sub-study. So not only am I providing more data about my own body and my activity, I'm actually using that data to help me and my doctors manage my own health. So that's a huge benefit as well.

But there could be negative impacts from a trial as well. Luckily, Paxlovid is relatively well-known. We know a lot about its side effects and effectiveness for acute disease. So I wasn't super worried about negative impacts on my health. But as a quick counterpoint, I also looked into a cardiac rehabilitation trial. But there's no way I would participate in that because it would have required significant physical activity. That's the one thing my doctor told me I should absolutely not be doing right now. So it's really important that studies are informed by clinical best practices as well.

Okay. Next, let's talk practicality. And I think Michelle hit on a lot of these topics really well. The thing that's most important to remember from my perspective is that most of us with long COVID are operating at just a fraction of the energy capacity of the patient you might be used to. That means we need you to respect our time and focus on and track the things that matter most to us. And I found that the study has been pretty respectful of my time. Five visits in three and a half months, and they are even in the process of adapting their protocol to allow for more virtual visits. So that's a huge plus for many of us. I also appreciate that they're tracking many of the outcomes that are important to me fatigue, cognitive symptoms, and impact of long COVID on my daily life. I wish there was more about post-exertional malaise, but I'll take what I can get.

Finally, let me talk about compassion. You've heard a lot of stories today about some of the just dreadful experiences that we're having in the healthcare system. And so honestly, one of the things I've appreciated most about the study I'm in is that everybody I've interacted with has been caring and has validated my experience. There's no gaslighting. And even when I might be more knowledgeable about a topic than other folks, there's appreciation and curiosity and validation. It feels more like an actual collaboration where we're invested in each other's health and success, and that feels really good.

The thing about compassion is you can't fake it, whether it's in your recruitment materials, email or phone interactions or even seriously on clinicaltrials.gov. We are very good at reading between the lines and honestly, we want to work with the folks who really care about us. Compassion is a balm that gives me hope and makes me confident that we will find answers. It costs you nothing, but it means everything.

So to wrap up, I just want to say we're really eager to collaborate with researchers. We need you as much as you need us. So let's be impactful, practical and collaborate together with compassion. Thank you.

MS. BENT: Thank you, Ezra. I definitely feel like there's some commonalities so far between what you were saying and what Michelle was saying, and I think that you're making some really important points.

And so now I'm going to turn to Liza. Liza, if you wouldn't mind going ahead and kind of sharing your thoughts with us, we would really very much appreciate it.

MS. FISHER: Hi. Yes. Thank you to the FDA for hosting this panel, for all of the clinicians, researchers and healthcare providers that are taking on this subject matter and cause, and especially to all those dealing with long COVID or some other post-infectious illness living at home, using those precious spoons, trying to find information here.

My name is Eliza Fisher and a little bit of background about me. I'm 38. I'm from Houston. I did get COVID in 2020, and prior to that, I was a very active lifestyle, international flight attendant, part-time yoga instructor. I was independent living, and I got COVID. I struggled to find healthcare. I ended up in the ICU five weeks later and a rehab hospital for three months after.

MS. BENT: And if you wouldn't mind just slowing just a little bit down so that interpreters can get things, I appreciate it. Thanks.

MS. FISHER: Yes, sorry. Along that time, I had the gambit of symptoms that we've all heard and that led me down the path of treatment and diagnoses similar to the experiences that you previously heard today. Additionally, I've also experienced the transition from different socioeconomic status in the world and dealing with different types of disability, private and SSDI, Medicare and transitioning from independent living to dependent living.

As far as my perspective on clinical trials, one of the things that is unique about my case is I did have a positive PCR test and a lot of medical documentation in the beginning. So personally that hasn't kept me out of a lot of trials, but it is something that is very common in the community. I also had a caregiver that was able to help me with transportation and reminders to fill out paperwork and helping me not only in preparation for the different appointments, but in the different appointments as well.

Things that have made clinical trials more difficult. I think in general, anything around accessibility and privilege and mean and root cause is a lot of just financial access and accessibility. Anything that is in-person is extensively more difficult than anything that can be telehealth or done online and it also continues to add to the cost associated with participating in trials, as you've already experienced a loss of either employment and income or healthcare coverage.

An example I would be -- an example I had was in 2021 a Houston company tried to start a stem cell trial and when I called in to see if I was able to participate in it, I was told that you must biobank your stem cells. They offered different packages ranging from $3,000 to $10,000. After the biobank was made, then I could participate. However, being I was working on disability, this cuts trials like this out and a significant population affected by these medical conditions just can't participate in a trial like this.

Another experience, I tried to get in a clinical trial with CytoDyn for leronlimab out to Texas because it was only having certain locations. We found a trial site, researcher and everything to connect and had a diverse population here. However, that wasn't able to be successful for still reasons I don't entirely know.

Different things that have made trial participation difficult, also off label treatments that I may currently be on, like steroids, may mean that you don't meet exclusion criteria. And there's other problematic exclusion criteria in clinical trials that involves the activity ranges for vitals. They're just not sensitive for this nuance of patient population.

Then any side effects weighing into my decision. To be perfectly honest, in my personal case, every time I read a list of side effects I thought, oh, that's my Saturday. So I think that there's a lot of people who are just willing to try anything like myself, and the side effects aren't necessarily as prohibitive. But when you go into a patient community and you find other people who have been trying it, you see something that could possibly trigger an increase, it may cause you to refrain. But I think adjusting these interventions with like micro dosing and slow titration schedules may be able to allow people to access these more.

Other considerations, root source being financial and physical support. There was a section on regarding a placebo. If a placebo was offered in a trial and the trial did prove that the treatment was positively advantageous, I would consider doing the trial and risking a placebo if I knew that the advantageous results would be provided after the trial.

And overall outcomes that are most important to measure in trial settings are energy level, particularly dealing with post-exertional malaise, fatigue, brain fog, neurocognitive function, pain, spasticity, any and all related symptoms to autonomic dysfunction and performance of daily life activities.

MS. BENT: Thank you so much, Liza. I really, really, really appreciate that. So now we're going to turn to Ryan to have Ryan. Hi, Ryan.

RYAN: Hello. Thank you for having me.

MS. BENT: Thanks. Please go ahead.

RYAN: So I'm Ryan. I have had long COVID for about a year and a half. My primary symptoms have been brain fog, post-exertional malaise, sleep issues, heat intolerance, tinnitus and epilepsy. And so I think one of the most important aspects of any sort of clinical trial is making sure to measure biomarkers properly and to make sure that they are properly controlled because my symptoms have improved sort of moderately over time. So sometimes I'll see like a study that's been trialing a medication for six months and they've seen moderate improvement, but that's my experience without medication.

So I think controls are one of the most important parts of clinical trials and I think measuring biomarkers is also really important because I know that there are sort of these observational trials happening right now, but we also need medications right now. And having a clinical trial that measures biomarkers while providing medication, you can see that if the symptoms improve, also if the biomarkers change at all, especially since COVID probably has -- it's a complex multisystemic disorder. It probably has multiple causes. So you could even focus in on if a medication only helps, say, 30 percent of people who take it, which 30 percent, which biomarkers are associated with that, which biomarkers change on the medication.

And then also it might be important because if some biomarkers improve but some symptoms don't, again, COVID is a probably multisystem disorder, so something that doesn't provide a lot of help on its own might be like a critical part of a larger therapy treating multiple issues at once.

But that said, I do think it's also critically important to measure subjective outcomes as well on post-exertional malaise, brain fog. These are some of like the most debilitating symptoms that we're all having and there's no good biomarker proxy for them yet. So it's very important to include that in any sort of study on how effective medications are.

Sort of biomarkers I would be looking for would be sort of vascular ones involving things like microclotting or endothelial dysfunction, immunological biomarkers like T cell disturbances or cytokines that are associated with perhaps chronic infection or just immune dysfunction in general as well as neurological markers like imaging tests or neuroinflammatory markers, indicators of blood-brain barrier dysfunction, things like that, as well as metabolic markers like disruptions to lipid metabolism, oxidative stress, increases in anaerobic respiration.

And I do think it's also important to try testing multiple medications at once in the same trial, because, again, this is probably a complicated multisystem disorder. So it would probably be useful to have something where, say, if you have two medications, like immune dysfunction might be causing some of the vascular issues, and the vascular issues might sort of prevent the immune system from sort of pulling itself together and clearing out the rest of the virus. So you might need something to treat both of them at the same time. So seeing studies that would, for example, have a control group, a group receiving something for vascular issues and a placebo, a group that's taking an antiviral and a placebo and a group that's taking both at the same time, seeing how sort of these different medications, if they have any sort of synergistic effect.

In terms of what I look for specifically when I'm looking for a study, due to my brain fog issues, I do not feel comfortable driving. So I really have to go to an area that is accessible by public transport. I'm in the RECOVER program or the RECOVER study at Mount Sinai. And being able to take public transport into New York City has helped a lot. I also receive reimbursement for public transport costs, which also helps because I have not been able to work. And another part of the study that I like is that you do get your results back, which is also useful just for my own personal medical -- I can provide it to medical providers and make further treatment options based on that.

But I think sort of Liza touched on this a little bit, like I can't work or really even live like a normal life. So I'm at a point where I would be willing to try really a lot of clinical trials simply because there's a level of sort of desperation and this idea that we need sort of treatments as soon as possible. We've all been trying to do our research and everything, but that's not really, I think, a sustainable option in the long run. So, yeah, I would like to see more of these trials going forward.

MS. BENT: Great. Thank you. Thank you, Ryan, and really appreciate that. And I continually forget to mention that again, that this meeting is being recorded and will be posted on the FDA website. So for those of you who may not be able to stay through the duration of a six-hour meeting, which we know is exhausting, please know that the meeting will be recorded and will be available. It will just take us a few days to get everything up and running.

But with that, let me turn over to Lisa. Lisa, to share your thoughts on this. I know you have a lot and you've thought a lot about this, so I really appreciate you joining us. Please go ahead.

MS. MCCORKELL: Thank you, Robyn. Hi, everyone. My name is Lisa McCorkell, and I've had long COVID since March of 2020, and I'm one of the co-founders of the Patient-led Research Collaborative, who are a group of people with long COVID who conduct research on long COVID. I am one of many millions of people with long COVID, and our numbers continue to grow as COVID spreads. While I am generally a mild case of long COVID, my symptoms impact my everyday life, having developed postural orthostatic tachycardia syndrome, post-exertional malaise, cognitive dysfunction, fatigue and premenstrual dysphoric disorder.

As I've tried to participate in clinical trials thus far, I've run into a few barriers. First, there's just not enough happening right now, particularly given the scale and severity of long COVID. Second, despite being heavily involved in long COVID research myself, it takes significant effort to even find clinical trials. Researchers need to better promote their studies to the patient population and not focus solely on recruiting through long COVID clinics, which have many barriers to entry. And third, because I got COVID so early and was not able to be tested, I'm unable to participate in any clinical trials that require a positive COVID test for inclusion.

And as Michelle said earlier, it won't just be me who is excluded. A minority of COVID cases have actually been properly documented by PCR due to inaccessibility and also PCR tests having high false negative rates, particularly among women and people under 40 years old. And antibody tests are also not reliable, as women and people with mild infections are more likely to not seroconvert and serorevert. It's critical for clinical trials to, at minimum, have an arm that allows for clinical diagnoses of COVID so that the millions of people like me can participate.

If I am eligible and can find clinical trials though, there are a few things I would consider before signing up. First, the intervention. As someone who has post-exertional malaise, I would not participate in a clinical trial that is testing graded exercise therapy, as my own baseline has decreased due to exercise, and research shows that this harms people with post-exertional malaise.

I would prioritize participating in clinical trials that are testing interventions that have a base and existing evidence on long COVID and other infection onset illnesses, and ones that are of importance to the patient community. These include antivirals, antihistamines, anticoagulants, JAK/STAT inhibitors and immunomodulators. I would also consider the side effects of the intervention, particularly if there is a high likelihood my symptoms could be permanently made worse on the intervention. But I would be willing to risk some side effects for drugs that are showing promise from patient anecdotes and that test a promising hypothesis.

Due to limited energy as well as risk of getting reinfected with COVID, I would be more likely to participate in a decentralized clinical trial that is fully remote or requires only a few clinic visits. But if the evidence behind the drug is strong and of priority to the patient community, I would consider more in-person clinic visits with additional travel that is reimbursed. However, it's important that trials also give the option to have at-home visits to ensure (indiscernible) COVID patients can participate.

I would consider the clinical trial design, whether patients are stratified by phenotype and whether the design is considering and measuring differences based on illness duration, where patients are in their menstrual cycle, any mast cell reactions, post-exertional malaise from clinic visits or the intervention itself and any potential impact of or to endothelial dysfunction and organ damage.

I would prefer to participate in a crossover trial where everyone receives an intervention. But I would also personally be okay with the risk of receiving a placebo as long as I can continue taking other medications and supplements that currently help me somewhat manage my symptoms.

In terms of outcomes to prioritize, I would want a trial to ensure clinical significance that the intervention has a meaningful impact on my life. Ways to measure this include quality of life measures, standardized tools for symptoms and conditions like the DSQ-PEM and COMPASS-31 and the severity of our most impactful symptoms. And while it is often argued that there are no specific biomarkers for long COVID yet, there are tests that often come back abnormal in people with long COVID and are often pulled from research into overlapping conditions and comorbidities like ME/CFS and dysautonomia. Examples of these include cerebral blood flow, natural killer cell function, T cell functioning, microclots and levels of reactivated virus.

Overall, there are millions of patients who desperately need well-designed, accessible trials testing therapeutics that are a priority to the patient community. Excuses of no definitive biomarker or murky endpoints are not acceptable. There are ways to do this well, and we need to do it now. Thank you.

MS. BENT: Thank you, Lisa. And so I want to just take a moment to thank all of our panelists for really sharing their thoughts and sharing their stories.

So thank you to Michelle and Ezra, Liza, Ryan and Lisa. And I think that we may have some follow-up questions from my FDA and HHS colleagues. So I hope that the panelists -- I think I gave you a heads-up that we might have some clarifying questions or some follow-up questions. So I hope you'll be willing to consider answering some of these questions.

So with that, let me turn to Dr. Habal, one of my colleagues, to ask maybe the first question for panelists. And if you're willing to answer, please either just, like, raise your hand or turn on your camera or whatever it is that signals to me that you're willing to answer. Thank you.

DR. HABAL: Good afternoon. I wanted to thank you all for sharing your experiences today. And I have a two-part question. I heard several panelists mention that brain fog is a common symptom that you are experiencing. So for the first part of my question is, how do you measure brain fog in your words and experiences? And the second part is, what would you all consider is a meaningful improvement either in this or in any of the symptoms that you had experienced? And thank you again for your insight.

MS. BENT: Great. Thank you. All right. So we'll start with Michelle, and then we'll go to Ryan.

Michelle, go ahead, please.

MICHELLE W.: Hi. So one of the ways we measure brain fog in our house is I have a regular activity that I do with my daughter. I give her 10 letters and then I give her five minutes, and I ask her to come up with as many words as she can in those five minutes. And so it's looking at her cognitive function, her language abilities and we've done it enough times that I will repeat them so I can see it's not just the letters that I gave her. So that's one of the ways.

We also have kept track, one of the biggest things that happens for her is that she does what they call paraphasia, which is where she might want to tell me to close the door one day, and instead she said, can you please close the bananas. So she uses the wrong words for things, and so we keep a running list of those to have an idea of is it happening more frequently, is it happening less frequently, are the words becoming similar to the words that she actually meant. Bananas and doors have nothing to do with each other, but bananas and oranges would be a positive sign for us. Those are some quick and easy tests that we do at home just to keep an eye on what's going on with her.

MS. BENT: Great. Thank you. And do you have an idea, Michelle, before I move on to Ryan, do you have an idea of what would be a meaningful improvement as far as --

MICHELLE W.: Yes.

MS. BENT: If you couldn't make it completely resolved, what would meaningfully better look like?

MICHELLE W.: Her original life goals were to become a doctor. She is aware at this point that without significant recovery, that may not be a possibility anymore. She has documented significant cognitive decline and change from her baseline status. And so if that's no longer a possibility, at a minimum, we are looking for her to be able to return to school. She can't be in school right now. A half hour of cognitive exercise, and she's spending hours recovering from it. So being able to tolerate returning to school would be the most meaningful improvement for us.

MS. BENT: Thank you. Thank you. Let me now turn to Ryan.

RYAN: So for me, this sort of goes back into why I was saying that subjective biomarkers are also really important to measure because I don't know of, like, a good test specifically because my brain fog also ties into my post-exertional malaise. So I know that I am at least somewhat capable of putting it together more, like I'm doing sort of right now and that might show a more normal test result or something, but I'm going to pay for it a lot more later. Like this evening, I'll probably just have to sort of lay down and not do too much, possibly even tomorrow as well. So for me, I think it would be very difficult because I don't know the best type of objective test to sort of run. I do know that when I do have brain fog, sometimes I can have trouble with reading comprehension. I tend to sort of pause more during speaking and things like that.

But yeah, like I said, unfortunately, it is very sort of subjective and I can especially sort of force myself to be more cognitively present if I have to be. In terms of what improvement looks like, I actually started taking guanfacine as a medication because I saw a case study that seemed to improve brain fog and that actually has improved my symptoms. I noticed that sort of when I do exert myself mentally, I'm able to do it for a longer period of time. And when I do crash, I tend to recover quicker.

So I do know that there is improvement possible because I have experienced it, but it is very difficult to sort of, I think, measure and also to sort of just even put into words. So I think that just having subjective measures of brain fog might be and whether it improves or not might be an important aspect of treatment in clinical trials.

MS. BENT: Thank you. Let me turn to Ezra.

MR. SPIER: Hey. Thanks so much. Really good questions. In terms of measuring brain fog, I want to be a little bit blunt. I'm looking to you, the clinicians, to tell me how to manage this. I'm happy to share this. I appreciate you asking the question, but we are literally in a reduced cognitive state, so it's really difficult to even answer these questions, let alone give you some specifics.

That being said, I think what I've experienced is -- the two questions you asked are actually very, very similar. One really great way to evaluate brain fog and post-exertional malaise is about what we're able to do in our daily lives.

So I think about potential metrics like how much time can you spend standing during a day without a crash? How many hours of activity are you able to do? Are you able to sustain a one-hour phone call or a one-hour conversation without getting a headache? Really direct, concrete things, measuring kind of our ability to have daily activities I think would be highly impactful. And those are the same things that are meaningful.

I would love to be able to sit through a six-hour Zoom without having a crash tomorrow. I would love being able to go to a study, meaning without having to explain post-exertional malaise to a study coordinator. So I think that really basic day-to-day activities and what we're able to do is a fantastic way both to measure progress and, in turn, show progress.

MS. BENT: Great. Thank you. And let me turn to Lisa.

MS. MCCORKELL: Thank you. I'll just add a quick couple of things. Just in terms of objective testing, the Cogstate is a really strong cognitive assessment. The CNS Vital Signs, the CANTAB. So those are ones that we generally recommend for cognitive function.

MS. BENT: And do you feel that those measure things that matter to patients? The way that the questions are formed, they're measuring things that are important to patients? Because I think one of the things that we're really trying to get to, we know there are a lot of measures. Some measures kind of measure things that matter to patients, and some measures maybe not so much. So I think that that's kind of maybe -- I don't want to speak for Dr. Habal, but I think that that's kind of where we are going to as far as like --

DR. HABAL: Yes, I agree with you completely.

MS. MCCORKELL: Yeah. I think importantly, anything needs to test processing speed, which many objective tests aren't testing processing speeds. That's one of the most important things. And then in terms of a meaningful difference or improvement, that's why I think it's important to pair any of that with quality of life measures so that you can also get that viewpoint. So did it meaningfully improve for the patient, and is it improving their life and how they're going about living their life if they're able to work, do activities of daily living, that type of thing.

MS. BENT: Great. Thank you. And let me go quickly to Liza. And then I think we have one more question from one of my other colleagues. So, Liza, go ahead, please.

MS. FISHER: Thank you. I just wanted to reiterate a little bit of what Lisa said also. Those quality of life outcome measures are definitely important. I myself have been able to measure some of my brain fog and cognitive impairment because I got neurocognitive therapy and speech therapy. So I had a battery of assessments, neurocognitive assessments done several times throughout the last three years. One of those things when you said you want to figure out which ones are good, I would like to point out that the Beck's

Anxiety Index specifically has three questions that are skewed for those with dysautonomia. That's a really poor measure to use on this population. Thank you.

MS. BENT: Thank you. So, Dr. Habal, did that answer your question? Did you have any follow-up for that?

DR. HABAL: No. I just wanted to thank the panelists for their insight.

MS. BENT: Great. Thank you so much. So let me maybe turn to Dr. Karimi-Shah. Did you have questions for our panelists?

DR. KARIMI-SHAH: Thanks, Robyn. Can you hear me?

MS. BENT: Yes.

DR. KARIMI-SHAH: Again, thank you to all the panelists. I've been struck by all of your stories today, and I think you've described how helpful this is for you to be able to sort of come into this forum and recount what your disease process has been like and it's very helpful to us on the FDA side to be able to hear it as well.

I'd like to come at my question from sort of the other side of where Dr. Habal approached in terms of a clinically meaningful benefit. From what I've heard from all of you today, there are a number of disabling symptoms that you all experience, and these are striking to me. And I'm wondering, when we -- we obviously at FDA have input into clinical trial design and which drugs get used. We don't design the trials de novo. And so we're always trying to assess sort of the risk/benefit of a clinical trial to the patient. So I wanted to approach my question from the side of risk and ask what kind of toxicities would you be willing to tolerate and what would you not be willing to tolerate? Because this is something that we take into account when we look at clinical trial design.

MS. BENT: All right. We'll start with Liza.

MS. FISHER: Hi. Could you actually repeat that again? Toxicities?

DR. KARIMI-SHAH: Toxicities of investigational therapies, like in a clinical trial. Like what types of side effects or toxicities of a medication, if you were entering into a clinical trial, potential toxicities would you be willing to tolerate in terms of things that might be beneficial for your symptoms and what would just be outside the scope of what you would be willing to tolerate? Is that clear?

MS. BENT: So for example, if a medicine was going to cause you to have increased liver functions or a lot of nausea or a lot of pain or, I'm just making things up, but just low blood counts that would increase your potential risk for infection, anything like that, I think, is where you're going. Did I capture that a little bit, Dr. Karimi-Shah, or was that not what you were thinking?

DR. KARIMI-SHAH: Yeah, and I'm asking because the symptoms you all are experiencing are so multisystem and multidimensional. And so I'm wondering, I've heard a few comments like, we'd be willing to try just about anything at this point but then I've also heard some comments that caveat that to say that something that worsens another aspect of my long COVID that I'm dealing with would be unacceptable. So I'm trying to get a sense as to what, from your personal experience, what would you be willing to tolerate as a side effect and what would just be out of the scope of what you would be willing to tolerate in a clinical trial.

MS. FISHER: Okay. From my personal experience, I think because I did have a little bit more of a severe acute case, I am willing to tolerate a little bit more discomfort in managing pain things due to a treatment. And if there is some type of historical evidence that that would go away or dissipate within a certain period of time, that gives me more incentive to try it. I guess it's really nuanced, and it comes down to those small quality of life measures. Is my GI symptom going to be upset by this medication 15 percent more five days a week or 10 percent more three days a week? Those are the types of questions that I'm asking when I'm considering treatments.

MS. BENT: Thank you. Let me turn to Michelle.

MICHELLE W.: So in terms of being willing to risk, I think one of the first questions I would have is, is there treatment for these side effects? So let's say something's going to make you potentially make you really, really nauseous, but Zofran works really well to stop the nausea. For example, my daughter does take a medication that manages a symptom very, very well. The side effect can be severe nausea in the beginning, vomiting and other side effects. But we were able to combat the side effects.

Also are the side effects reversible? So let's say it does cause an elevated blood count or a risk of infection, but after six months that's reversed and you go back to baseline. That's more tolerable than something, let's say, oh, it can cause increased liver function values. And once they're elevated, they're elevated. We've done treatment that actually did cause severe side effects, DVTs, in fact. And it was a known risk and we took the risk. Unfortunately, she had the side effect and therefore had to stop. However, we brainstormed and tried to figure out how to continue trialing that treatment because it was working.

So if a treatment is working, the risks are much more palatable, as well as knowing that there is treatment or there's something we can do or after the study, the chances are very high that any side effects will be reversed. Also the opportunity, like we did with the cognitive rehab, is knowing that if side effects become intolerable, to leave the study. For my daughter, intolerable meant that she was sleeping 20-plus hours a day again. And we had managed that symptom prior when she was at the point where she literally could not be awake other than a couple of hours, we had to drop out of the study. So risk/benefit ratio.

DR. KARIMI-SHAH: That's exactly what it comes down to. Thank you for your answer.

MS. BENT: Thanks, Michelle. Let me turn to Ryan and then we're going to turn to some callers to hear some of their experiences. So Ryan, go ahead. Thank you.

RYAN N.: So when I think for some of the studies that are being mentioned that patients wouldn't want to do, I think from what I've heard in patient advocacy groups and stuff, a lot of them are related to things that have been tried for ME/CFS already and don't have strong support behind them. So I think for a lot of the studies where people are saying, I wouldn't really do this, I've been hearing it's been more like exercise therapy or cognitive behavioral therapy.

So I think part of that for some of those studies is that it's not necessarily just about the worsening of symptoms, but also is there a large body of research suggesting that this might not be an effective treatment. So I think that's one thing to pay attention to, if you're hearing patients saying, we don't want to do this particular study, or something like that.

But as for me and my own risk tolerance, as I mentioned, I've had long COVID for a year and a half. I've not really been able to maintain a job, a normal social life, the independence that I had before. So my risk tolerance would be pretty high, especially for a clinical trial. I be very much willing to deal with side effects, knowing that they might dissipate if I go off the trial or if my body has time to acclimate to them.

I think the biggest thing that I would have concerns about would be essentially the risk of irreversible side effects or death or something like that. For example, in anticoagulant therapy, I would probably want to have some sort of test to see if microclots are actually happening because going on anticoagulants when you have normal blood might not be like the best, and then that could cause like a stroke or something irreversible. But overall, in terms of, let's say, discomfort or reversible side effects, especially for just a clinical trial, and that's something that I'm not necessarily going to be on for the rest of my life, yeah, my tolerance for that is very high.

LARGE-GROUP FACILITATED DISCUSSION ON TOPIC 3

MS. BENT: Thanks, Ryan. Really appreciate your thoughts on that. So with that, I think we're going to give our panelists a little bit of a break and we're going to turn to our callers, and I think we will go first to Michelle on line seven.

Michelle, would you like to share with us some of your thoughts and experiences related to clinical trial participation? Maybe talk about what made it easier or what made it harder?

MICHELLE: Yes. Hi. Thank you. Thank you for having this meeting and for taking the time to include patients and also hear the feedback and move forward with some things. I have had long COVID for two and a half years. I had my first COVID infection in September 2020. My first infection was mild. One month after I had that infection, I started having constant chest pain. An ECG at my primary care revealed an abnormal ECG. Before I could check into this more, I got COVID again from a family member visiting us in November of 2020.

The second infection about did me in. It was so much worse. I had every symptom except a fever, and my oxygen was above 90 percent when I went to the ER urgent care. Of interest, my symptoms got better at about three weeks before getting incredibly terrible at four weeks after my second infection. I had elevated D-dimer for months. I had the abnormal ECQ, which persisted for over a year. I had collapsed veins. I had bilateral ground glass opacities, and I had very low white blood cell counts. But I'm in my 40s, early 40s, and no one would do anything except just send me home and say to stay hydrated.

Since then, I have done so many things to try to get better. Every inch I can get. I very much want to get better. I have tried and participated in two long COVID trials, NIH trials. Part of what allowed me to participate in these trials was the location and accessibility. I think that those three things, location, accessibility and visibility are really important. It's my hope that there can be coordinated locations to help reach people who want to participate in these trials, but they're not near a main center like the RECOVER Initiative. I'm not well enough to go fly to New York or to places where I could participate. So I think that that's really important, that there's possibly a coordinated approach.

I also wanted to mention regarding one of the panelists or the doctors had asked about toxicities and side effects. One of the things that -- there was no toxicities for either of the trials that I participated in. So it was an easy yes, because one was virtual and one was close by to me. If there was toxicities that were being possible from a drug that was being trialed, I think the thing that would affect me is could those toxicities cause permanent damage because that would be something that might turn me away, or if those toxicities would just be short-term damage or would get better once the drug was stopped, I would still consider trialing a drug.

So the other thing is the Mind Body study. I participated in a Mind body long COVID study. It was based out of Beth Israel Deaconess. I'm based in Milwaukee. So obviously this was a virtual study. It did help me with some of my muscle pain. It was accessible to me because it was virtual. Ideally, studies that don't include a placebo are better for patients, in my opinion, because everyone who has long COVID right now wants a chance to get better as soon as possible. Any studies are better than no studies. And I know that the placebo studies are often more highly regarded, but I think everybody so desperately wants to have a chance to get better because we're trying so many things on our own, and frankly, a lot of things aren't working.

I did participate in a COVID probiotic study on vascular effects at the Medical College of Wisconsin. I was able to participate in this due to location. I did receive the placebo, but I am trying the probiotic on my own, out of my own cost afterwards to see if it helps.

Ideal outcomes for me, studies would include reduction in fatigue, brain fog, neurocognitive dysfunction. One of the panelists mentioned misusing words frequently. Yes, that happens all the time. Difficulty focusing, where I had no difficulty focusing before, I was a magna cum laude graduate. Very able to focus and write a paper very effectively. I have chronic circulation problems now and vascular problems.

I still have noncalcified nodules in my lungs, vision problems, chest pain and breathing problems.

One thing that I'd like to add that I don't think was mentioned yet is I had no known risk factors before COVID that would have given me a heads-up that it was going to be so bad for me. And so some trials with specialized tests such as cytokine test, tomatine test, immunological tests, genetic testing, biomarkers to help understand more about what happened with me with COVID and why me and so many of us got so ill and aren't recovering. I would like to not just have a trial give me treatments, but I'd also like to know why the heck this has been so bad for me. I had no idea that it would be.

MS. BENT: Right.

MICHELLE: Of note, the last thing I'd like to add is that it is my hope that a drug like Evusheld, which is a long acting monoclonal antibody which may help with viral persistence, will be included as a treatment based on my and a small amount of other long COVID patients' positive experience. I received Evusheld in 2022 for my new post-COVID immune-compromised status because I had chronic low white blood cell counts after COVID, and I did not have that problem before. I found that Evusheld surprised me dramatically. It helped with my long COVID fatigue, lightheadedness and GI symptoms. It helped my fatigue so much that I was able to even complete something like mowing the lawn, which was just totally out of my realm before that.

I'd also like and hope that other drugs can be trialed and repurposed. At this point, to me, exploration is really important and new things aren't going to get discovered if they're not looked at and tried at this point. So I hope that long COVID treatments and medicines will be vigorously explored with expedited results and widespread locations for trials or coordinated locations to reach people in different areas.

MS. BENT: Thank you. Thank you, Michelle. Really, really appreciate your thoughts about that and really appreciate the detail that you went into. Let me turn now to Alice on line four.

Alice, I know you've been listening and I know you've been on hold for a while. I really appreciate your patience. Would you want to give us some thoughts about clinical trial participation and maybe what would be important for you?

ALICE: Yes. Hi. Thank you so much for taking my call and also to the FDA for holding this interactive meeting. For full disclosure, I am a physician who's been in practice for over 20 years, but I've also been very severely affected by long COVID since early 2020.

My brief comment is about the inclusion/exclusion criteria and outcomes measures for planned trials. In my personal case, unfortunately, SARS-CoV-2 caused documented organ damage in previously healthy organs, including brain, where I had an anoxic brain injury, COVID encephalopathy and a resulting TBI-like brain illness, in my blood, where I had a hypercoagulable state that had to be treated with anticoagulation, immune system where I've had dysregulation and impairment for about two years of the disease, in my heart and cardiovascular system where I've had several issues including clots in legs, lungs and brain, in my GI system where I lost my gallbladder and appendix seven weeks apart, in my liver and in my kidneys, where I had as bad as stage three kidney disease.

So some of these organ issues have improved or reversed, but others are still present. So as a result, I personally have not been a candidate for many of the clinical trials that have been proposed and are ongoing. I'll repeat, a healthcare professional with severe health issues due to SARS-CoV-2, and I have not been a candidate for many of the trials. The point is, long COVID can be associated with organ damage for some people, I suspect a larger population than we may recognize now. Some of the organ impairment may be fully detectable, like mine and your previous caller that had brain aneurysms and other organ involvement may not be apparent yet. And it's very possible due to the lack of longitudinal data beyond three years that we haven't appreciated the full extent of outcomes of this condition in the long COVID community.

So for clinical trials, I'd like the FDA to address not only palliative therapies for symptoms, but also definitive ones targeting underlying causes. But my main reason for calling in is to discuss inclusion/exclusion criteria for trials. So I'd like to ask the FDA to carefully consider inclusion of patients with acceptable degrees of documented or suspected organ damage. This would include patients who've been sick for a number of years, who may be more likely to display it as organ damage seems to appear over time.

And this recommendation may seem counterintuitive for some clinical trials, especially when testing interventions that have known potential toxicities. But I really would recommend careful consideration of including of patients with an acceptable degree of organ impairment in all trials where it's possible, just as we do in some other multisystem conditions in the rheumatology space and cancer.

And finally, for studying outcomes, in addition to safety and efficacy of plan interventions, I'd like to see trial endpoints include improvements in organ dysfunction as well as prevention of organ dysfunction in the future. That concludes my remarks. Thank you so much.

MS. BENT: Thank you, Alice. Really, really appreciate that. Let's take a brief break from callers. Let me turn to Shannon to see, Shannon, do we have any comments from the Web related to toxicities? I feel like we were talking about that a little bit before. Do we have any comments?

MS. SPARKLIN: Yes. Thank you, Robyn. We have received several comments to the webcast regarding the question about toxicities, and there's a range of answers that patients are submitting. Some are noting that they are not willing to accept any side effects that would make them sicker than they already are, while others are willing to accept any side effects or toxicities because they feel like they are at rock bottom right now.

A few comments. One comment that I'll read states that something that takes away any last functional aspects is something that they would not be willing to tolerate. For example, they were given a medicine that can cause tearing of tendons and they began to develop bruising around their knees and Achilles tendons in their ankles. They immediately discontinued that medicine because losing the ability to stand and walk, in addition to everything else that they had already lost, would be an intolerable risk.

Another comment noted that they would definitely not be willing to tolerate pain, headache, nausea or organ damage. And finally, a last comment noted some of the symptoms that they would be willing to tolerate would include mild symptoms that can be relieved through over-the-counter treatment. So that would include indigestion, nausea, mild pain and low level headaches, while other symptoms that they're not willing to risk or tolerate would include worsening brain fog where they would not be able to communicate and any small decline in function.

They also noted that they've tried many antidepressants that drastically worsen their function to becoming bedbound. And once they tried another new medicine two months ago and it caused digestive issues but helped decrease their pain. Thank you.

MS. BENT: Thank you, Shannon. I know that we're getting a lot of comments into the webinar and we really appreciate those comments. Let me turn back to the phone. I think we'll go to Trista on line two.

Trista, would you mind sharing your thoughts about clinical trials?

TRISTA: Thank you.

MS. BENT: Thank you.

TRISTA: Yeah. I am entering month 38 of long COVID. I was fit with a healthy lifestyle and no preexisting condition when I was hospitalized three times in March of 2020 in New York City, and when I arrived at the overcrowded EE, I was already in sepsis and experiencing my first what my chart called a cardiac event. I was mistreated with the high dose hydroxychloroquine and azithromycin five-day protocol. I then had a neurological event which cannot be evidenced on modern imaging scanning technology, which caused me to lose my verbal fluency and ability to speak for seven and a half months.

Since then diagnoses of POTS, ME/CFS, hyperacusis, tinnitus, seizures, aphasia, PTSD, cognitive decline and fragmenting, otherwise called this silly minimizing term brain fog, depression, anxiety and other things I can't remember because memory loss. My improvement plateaued at the one-year point. And by the 18-month point, I began experiencing new and worsening symptoms, even with some treatments having previously helped.

Just researching and applying for participation in clinical trials on my own through the .gov website is extremely difficult cognitively. I tell every specialist I see in person that I am willing and interested in participating in clinical trials and they all just send me to the website to DIY the process.

I have participated in one clinical trial at significant personal financial cost, requiring personal loans from friends to cover travel and accommodations as it was in Southern California and I am based in Brooklyn. I did experience temporary improvement in one aspect of my symptomology, benefits which waned as both felt by me and reflected in the tests conducted 30 days after the end of the treatment period. Since then, those improvements have disappeared altogether. I cannot afford to continue that treatment protocol on my own out of pocket.

This was a study of long COVID women specifically and according to the lead science researcher, there was not one participant whose reproductive health and menses cycle had not been significantly impacted by long COVID and also by the bivalent vaccine. This was not the specific subject of this trial, but a secondary discovery of data affirming my own patient experience.

I firmly believe we need more studies specific to the reproductive health in long COVID women. Whilst in one study we cannot usually participate in another clinical trial without interfering with both baseline and treatment result data for that other trial. I am disqualified from other trials due to any one or combination of the ten prescription medications I am on from my neurologist, cardiologist, psychologist, pulmonologist, GP or pain management doctor, all necessary due to COVID.

Also, I cannot participate in any trial that includes graded exercise or the likelihood of worsening my symptoms and putting at high risk of stroke, heart attack and increased seizure-like activity I got from COVID, and many of the eligibility requirements are for patients who have had a COVID positive test within the past year only, leaving those of us in the first wave infected behind.

I want my body's data to inform medical

interventions through participation in as many clinical trials as possible. But I don't have the privileges of financial wealth, nor help in daily life activities or the cognitive efforts of self-tracking and recording my responses to the treatment. The lack of accessibility is a significant barrier and I agree that quality of life, independent functioning and daily activities and an improved life expectancy are important outcome metrics to prioritize.

In terms of the risk of toxicity, we're already on the edge of death, so frankly, anything not already proven to kill me immediately, I would try.

MS. BENT: Thank you. Really, really appreciate that feedback. Let me turn to Rachel on line one.

RACHEL: Hello?

MS. BENT: Hi, Rachel. I know that you've been waiting for quite a while. I know we all would really want to hear your perspectives on clinical trial participation. I would ask that you keep it as concise as possible just so that we can get to maybe one more caller before we are wrapping up the meeting. Thank you so much for calling in.

RACHEL: Of course. Thank you. Hi. This is Rachel. I have had long haul COVID since December 2020.

There are lots of types of long COVID. I have several of them, but the one I'm going to talk about right now is ME/CFS. A year ago I was too exhausted to feed myself. It was before my CFS diagnosis. I lost 20 pounds in ten days because I couldn't move well enough to feed myself. It's very hard to access treatment and I'm really lucky that I've been able to.

I'm going to ask for two things today. One is that I ask that consideration of trial designs look at treatment for conditions seen in long COVID and other post-infection conditions, things like what I have, ME/CFS and POTS, that would enroll anyone with a condition regardless of the trigger, whether it was COVID or not. These are existing communities of patients and we need to learn from them. I need to learn from them.

I am very, very lucky and very privileged to have access through a long COVID clinic to an ME/CFS clinic. Last summer, I started low-dose naltrexone and it immediately significantly improved me. I was stage five and went to stage four fairly quickly, which meant that I was no longer bedbound. Not being bedbound is awesome. I also started low-dose Abilify last fall and I'm 80 percent back to whole. And there are no active clinical trials looking at these conditions, these medications, and none looking at them in combination either.

We need government funding for clinical trials on these medications because for some people they can create a significant improvement and these aren't going to be highly profitable things to drug companies. So we need federal support to be able to do this.

I have been asked to participate in a number of clinical trials, as many other callers have echoed. Some of us are desperate and terrified, while exhausted. We will do a lot to participate in our care and to participate in furthering the knowledge in the field. And I've declined clinical trials because of the economic precariousness that has been introduced into my life because of long COVID.

There was one clinical trial that sounded great. I would effectively be subsidizing it because the small stipend didn't even cover the cost of gas. So I'm willing to put a lot in. But many of us are now experiencing a lot of economic precarity because of our conditions.

And then when clinical trial results are available, I have had to be far too strong of my own patient advocate to be able to just stay alive and get out of being bedbound. We need a different flavor of outreach, one that's more rapid and more thorough once clinical trial results are out so that more and more medical professionals can be aware of the news of the developing field.

And the last thing I want to say is that it's really important the clinical trials look at the effect of treatment on people who represent the full complexity and the full diversity of the large long COVID community. Lots of us have preexisting chronic illness or disability, looking at the frequency of people with autoimmune and complex chronic conditions. Clinical trials need to take into account the diversity of participants and put extra effort into that. Thank you.

MS. BENT: Thank you, Rachel. So we have just 13 minutes left of the meeting. I'm going to turn to our final caller, Jillian, on line three. We're then going to turn to Shannon for a wrap-up of the comments that we've received on the website and then to closing remarks. So I thank you all. We have about now 12 minutes left, and so let me turn to Jillian. I know you've been on hold for a long time, so I really appreciate that and please go ahead.

JILLIAN: Oh, my gosh, thank you. I was just going to write you my stuff, so I wasn't sure what I was doing. Okay. Thank you so much for holding this, to the FDA for today's program. I've had long COVID for three years, healthy, athletic, no preexisting conditions in NYC. Now I'm disabled and on SSDI, living with my mom. I'm in a 50-person independent research group of science-minded long haulers, so I hope that some of my comments represent some of their thoughts as well.

The focus of this panel is trials, not studies. So I was going to say I hope we can steer away from RECOVER as a topic, given it's a study, and I direct you to the recent Stat article detailing many of its serious failings and need for reform. The treatments that have been mentioned today are Band-Aids, and I hope that trials will focus on cures.

I would also note that from a previous caller's remarks, PTSD is not holding me back from getting better. This is a physical, progressive disease. We need trials for viral persistence for a cure yesterday. Viral persistence has been largely proven already. There are trials and studies that could be done with cats for FIP, feline infectious peritonitis, for example, which is a similar coronavirus. I urge the government to explore this, as there's already much evidence and research there.

For humans, there are several antiviral

possibilities to trial that the research community is aware of. We need a variety of extended trial and titration times. Fifteen days of Paxlovid isn't going to cure people. We already know that. These, quote, trials seem disingenuous at best. Emphasizing Liza and Lisa's opening remarks, many of us do need logistical help to participate, and in response to Dr. Karimi-Shah's question on toxicity, and similar to many panelists' replies, while I wouldn't want to experience permanent or irreversible damage from a trial, otherwise, my symptom threshold is high and I'm comfortable taking risks given my desperation.

Echoing others' comments as well, placebo studies seem like a waste of time given the urgency of this crisis. And lastly, we need people -- to let in people who got COVID before PCR tests because we make up a huge number of the population of patients.

There are several other treatment options that my group has been looking at that we care very much about and think are serious contenders for symptom improvement, such as cerebrylysin and other peptides with proven safety and tolerability, such as ARA 290, BPC 157, ANI third for people which seems to have potential for MCAS, SS-31 for mitochondrial dysfunction. I'd also note piracetam. The fact that this isn't available as a drug for people with cognitive issues is almost criminal. It's been around since the '80s and it's about time that it has a trial to make it available.

Drugs that target the immunomodulating factors associated with damaged GABA receptors is prevalent in people with long COVID. That's another one. Anti-inflammatory drugs that lower IL1Ab and IL6 is very important.

Drugs that address decoupled protein receptors such as CC 007, which is currently being trialed in Germany, why is the United States not doing that? Trials that could potentially address what we see in publications referred to as persistent spikes or partially replicating spikes is also important, especially if this is playing a role in driving systemic inflammation.

MS. BENT: Jillian, I'm going to ask you to -- I need to ask you to maybe focus on maybe one more topic.

JILLIAN: Sure. I'll close. Yeah, I'll close by saying that Pilates, GET, CBT and mindfulness are not going to cure us and in fact, these trials will hurt us and spin a false narrative about long COVID. We already know this from decades of destructive research for

ME/CFS, multiple sclerosis, et cetera. And lastly, I would warn the meeting administrators of special interest groups like the insurance industry pushing their own agendas and skewing your data. Thank you so much.

MS. BENT: Thank you, Jillian. And thank all of you. To those of you who we weren't able to get to on the phones today, I really do apologize. Please, please consider submitting your comments to the public docket because your thoughts are important to us.

Now I'd like to turn to Shannon to share maybe some final comments that we received via the Web before turning over to Rear Admiral Iademarco to provide closing remarks. So Shannon, please, go ahead.

MS. SPARKLIN: Thank you, Robyn. Just to mention, the perspectives that have been shared today that maybe we haven't been able to get to will be reviewed and incorporated into the meeting summary report.

But regarding some of the themes I've been seeing in the written comments related to clinical trials, some themes have been that it's difficult to access trials, especially for rural populations, and that there is a desire for virtual trials or less clinic visits. There's also been a key theme regarding inclusion criteria to make clinical trials more accessible to people with preexisting conditions and specific symptoms of long COVID.

A few important outcomes that people who submitted comments mentioned are reduction of fatigue, reduction of post-exertional malaise and reduction in brain fog.

One thing that a commenter noted would facilitate their participation in a trial would be location, time commitment, and out of pocket costs. And that same commenter noted that if something ends up being only 5 percent impactful, that is a huge improvement for them.

One commenter noted the factors that enabled them to participate in a clinical trial included reimbursement for transportation costs, the fact that the trial was close by, low physical and mental effort and the factors that made it more difficult for them to participate included the trials that focused on exercise or physical activity that made their symptoms worse and where the study locations were hard to get to or expensive.

Finally, another comment mentioned that many long COVID patients are presenting as immunocompromised or with immune dysfunction. However, many settings, including hospitals, have dropped mask mandates, and this has made participating in clinical trials significantly more dangerous for these patients, particularly as they see how reinfection is associated with increased risk and worsening of symptoms. And they would appreciate mask hearing in hospitals and telehealth or virtual options to limit this risk for long COVID patients who are choosing to participate in trials. Thank you.

MS. BENT: Thank you, Shannon, for, as always, providing a very comprehensive overview of the comments that we've received. So before I turn the microphone over to Rear Admiral Iademarco, I just do want to acknowledge that this was a very long meeting. And we understand that for those of you who are suffering from long COVID, particularly with the aspects of fatigue and post-exertional malaise, this meeting was a lot for you. And we very much appreciate you taking the time to participate and share your experiences with us. They are very meaningful.

And so with that, I am happy to turn over to re Admiral Iademarco, the deputy assistant secretary for science and medicine at the U.S. Department of Health and Human Services, who will be kind enough to provide us with closing remarks. Admiral?

CLOSING REMARKS

DR. IADEMARCO: Okay. Good afternoon. Just want to make sure the sound check is okay. I haven't spoken for a couple of hours.

MS. BENT: Yes. We can hear you, sir.

DR. IADEMARCO: Okay. Good. Well, I want to thank everyone, and there's no particular order. Doing this is hard, and I've been in biomedical science and public health for several decades, and I think we're getting better at it. But it's still a learning process. And I want to applaud the FDA and all the participants for working together for a very respectful, constructive exchange. And it's not comprehensive, it's not complete, and it's not perfect, but I think it was done extremely well.

FDA, in their opening comments, explained their evolving journey in this methodology. And of course, we all applaud that and encourage them forward. And I know firsthand how this information fits together with what everyone's trying to do, and that is to improve the outcome of patients with long COVID and associated conditions.

I want to also note, I don't know if we mentioned this earlier, that there were people from the CDC and the NIH on the call listening firsthand. And of course, there'll be notes and recordings as described that will help those scientists. And it really is an all of government approach, not just within NIH with the different organizations, the two I just mentioned with the FDA, but others, such as the VA and the DoD, who are doing research in this area. And then there's other smaller groups in HHS where this is very relevant, whether it be ARC, URSA, ACL, et cetera, and CMS for their role with insurance, for example.

There's been a lot of diversity and views here and in the people speaking, and you can just tell by any one person listening that it's a lot to pull together, that diversity is rich and robust and really important, but at the end of the day, we have to pull it together and make some steps forward in the right direction. And we may not always get it perfectly right, but that's what we're aspiring to do in HHS.

If you have suggestions on the process or the method that FDA used here, I'm sure they're all ears to that and there's various ways to respond. I'm looking through my notes here to make sure I hit everything I thought of. And I think so, so I'm really appreciative of all this, everyone's time. I learned myself listening to all the stories of the various patients and caregivers. So thank you. Shannon, back to you.

MS. BENT: Great. So thank you. I'm going to jump in again. So thank you, everyone. I hope that you have a wonderful day. I would like to just take this opportunity to thank all of the staff that put this together, all of the people working on the backend, our interpreters, our studio staff and all of the rest, but of course, most importantly, the patients who were really here to share their experiences. So thank you all, and have a wonderful day.

(Whereupon, the foregoing was concluded.)

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