

## CDC's 18th ME/CFS Stakeholder Engagement and Communication (SEC) Call

December 2021

3 p.m. ET

Christine Pearson: Good afternoon, everyone. Welcome to today's ME/CFS Stakeholder Engagement and Communications call, which we call SEC. Apologies for starting a few minutes late, we were having a couple of technical difficulties. My name is Christine Pearson, I serve as Associate Director for Communication in CDC's Division of High Consequence Pathogens and Pathology, which is where CDC's ME/CFS program is located. As you know, we host these SEC calls several times a year to provide information for people with ME/CFS their loved ones, clinicians and anyone else interested in the disease as part of our regular outreach and communication activities.

Our goals on these calls are to provide updates on the work of CDC's ME/CFS program and for you to hear from external experts in the field. Today we'll hear program updates from Dr. Elizabeth Unger. She's from CDC's Chronic Viral Diseases Branch. Then we'll turn it over to our guest speaker from Stanford University who will discuss ME/CFS and long COVID.

After Dr. Bonilla's presentation we'll have a Q&A session. During today's Q&A you will have the opportunity to ask questions through the webinar platform or by phone if that's how you joined today. We'll provide more information on that when we get to the Q&A session.

Before we start, I'd like to remind everyone the call is open to the public so please use discretion in sharing personal information. And we're recording this call so please disconnect now if you are concerned about that. We will post a transcript and video as soon as possible after the call.

Now we'll turn it over to Dr. Unger to start the program. Welcome, Dr. Unger.

Dr. Elizabeth Unger: Thank you very much. I'd like to welcome you to the 18th, hard to believe, Stakeholder, Engagement and Communications call, CDC's forum for regular communication with the ME/CFS community. I'll present some updates on CDC's ME/CFS activities and Dr. Hector Bonilla will share his presentation. We'd like to extend a warm welcome to Dr. Bonilla and

thank him for taking the time to share his experiences working with ME/CFS patients.

If you have suggestions for speakers or ideas for other topics, please email us at [mecfssec@cdc.gov](mailto:mecfssec@cdc.gov). This is also the address to use if you'd like to be added to our email notifications about upcoming calls.

Moving on to updates, the CDC ME/CFS program recently held the third Roundtable meeting in mid-October focused on encouraging partnerships and collaborations, titled "Working Better Together." While our prior roundtables were held in person, this was held virtually due to COVID restrictions. Our contractor, McKing, was able to use the Zoom platform for sessions and created breakout groups for small group discussions. They also created an informal networking session to give people a chance to know each other a little bit.

We appreciated everyone's flexibility in adapting to the new format and hope that future sessions will once again allow us to meet in person. In preparation for the Roundtable meeting, McKing held small group phone calls with members of the ME/CFS community to get their feedback on partnership experience and ideas for discussion. Based on this feedback, the meeting focused on three topics, healthcare, workforce education, surveillance and expanding the science, and awareness and stigma.

Over the course of two afternoons, Roundtable participants heard presentations from patient organizations, healthcare providers, professional organizations and federal and state agencies. On the first day Division Deputy Director, Jennifer McQuiston welcomed meeting attendees and I gave a presentation of overview of work being done by CDC's ME/CFS program. Tim McCleod, Senior Policy Analyst, and Donovan Newton, Associate Director for Policy in the Division of High Consequence Pathogens and Pathology, presented information to help meeting participants understand ways in which CDC can have successful partnerships while adhering to policy rules and guidelines. Presentations on successful partnerships from other areas of CDC rounded out day one. Judith Griffith of HIV Prevention, Wendy Ruben from Birth Defects and Developmental Disabilities, and Michele Walsh from Population Health, all provided insights into how successful partnerships have worked for their CDC programs.

The second day consisted of virtual breakout groups divided by three topic areas. McKing asked attendees to rank their preference of topics and they were split into groups. As a floater I was able to pop into each of

the breakout groups and I found the ideas and suggestions interesting and helpful to envisioning future partnership activities. The meeting concluded with a summary of ideas from each breakout group and potential projects. Information about this Roundtable meeting including the agenda, participants and presentations have been posted to our website. We expect the summary report to be finalized and posted at the beginning of next year.

As we have discussed before, the overlap between ME/CFS and post-COVID conditions, referred to as long COVID by many of those affected, creates an opportunity to better understand both conditions and to increase awareness among healthcare providers. We are supporting two studies that will follow people who have had COVID-19 including those who have had long-term symptoms and those who have fully recovered to better understand the illness.

The first study, COVID, Understanding the Post-viral Phase, COVID-UPP, will enroll patients three to six months following their initial COVID diagnosis. This study will follow patients who continue to have fatigue and other symptoms and a comparison group who have fully recovered using online surveys to gather information about their health for three years. This will allow a description of the course of the illness over time. A subset of participants will be invited for in depth clinical and laboratory testing that will allow comparison to ME/CFS.

Another study, Research on COVID-19 Long-Term Effects and Risk Factors, COVID RELIEF, will use electronic health records to investigate conditions and characteristics that increase the chance that a person will have a severe COVID infection or an infection that leads to long-term illness. A subset of patients will be invited to participate in a biomarker study that includes an interview and laboratory testing. We expect the results will help identify risk factors for persistent illness and may identify approaches for early intervention to improve therapy.

CDC supports a modeling project that will estimate the number of people in the United States with Post COVID Conditions and an implementation research project with a federally qualified health center to build the capacity of primary care physicians to care for patients with post COVID conditions, ME/CFS and other post-infection syndromes.

In previous calls we've mentioned our new collaboration with the Emerging Infections Program and California and Kaiser Permanente in Northern California. This is the STOP ME/CFS project, standing for

Surveillance To Optimize Protocols for early identification and subgrouping of ME/CFS. Most patients with ME/CFS are diagnosed after experiencing symptoms for many years so identifying individuals much closer to the time of illness onset is a key priority.

The first phase of this project is almost finished and involves a retrospective look at Kaiser's medical records to develop an algorithm to identify patients with prolonged fatigue who are most likely to be diagnosed with ME/CFS. In phase 2 the algorithm will be used to enroll a prospective cohort of patients. We will sample adults in four study groups. Patients diagnosed with ME/CFS, patients identified by algorithm as at high risk for ME/CFS, patients identified by algorithm as moderate or low risk for ME/CFS and patients with prior COVID-19. Data will be collected through a self-administered electronic survey at baseline and at one year and will be compared among the groups. Following up on people at elevated risk of ME/CFS will allow us to describe the early onset and early course of illness for ME/CFS. Including people with a history of COVID will allow the investigation of the occurrence of ME/CFS after COVID in comparison of long term COVID symptoms with ME/CFS symptoms in people who do not have a history of COVID.

The protocol for Phase 2 is under review by Kaiser's institutional review board and we expect to start in early 2022.

We've also continued to expand our healthcare provider educational offerings. Currently three continuing educational courses are available through Medscape and a new Spotlight course has completed filming via Zoom platform. The expert faculty included the moderator, Dr. Benjamin Natelson from Ichan School of Medicine at Mount Sinai and panelists, Dr. Donna Felsenstein from Harvard Medical School, Dr. Mitchell Miglis from Stanford University and Dr. Dale Strasser from Emory University. The course title is, "A Fresh Look at ME/CFS: Diagnosis and Management of a Multisystem Illness." We anticipate having this course launched in early 2022.

For educating medical students we continue to expand our work from the Standard Patient or SP learning and training program which has been published in the Journal of Translation Behavioral Medicine and MedEd portal. The SP project is a vital tool for educating medical students and residents on ME/CFS. We have produced six videos and published one of them in MedEd Portal. Currently we're working with Dr. Howard Selinger of Quinnipiac University to evaluate a pediatric ME/CFS module. This video consists of a video and slide presentation. Medical students at

Quinnipiac University will view this module and complete pre and post-session training to assess learning. When the testing is complete, we plan to publish the findings and disseminate the educational module.

Also related to pediatric ME/CFS, the phase 2 contract of the school-based active surveillance has been awarded to the National Association of School Nurses. The kickoff was held last this summer. Phase 2 will build upon prior work and expand our reach to include more schools in at least 10 states. Data will be collected on ME/CFS, post-COVID conditions, chronic absenteeism, and student health. Through this partnership project, we will also educate school nurses who could raise awareness of the illness and provide guidance on how to identify students with ME/CFS symptoms. Nurses can help students manage the illness and be successful in school.

Since the MCAM or multi-site clinical assessment of ME/CFS study was closed out in 2020, we have been working on five manuscripts for publication. Two of them are currently in review by journals. The first paper focuses on the work Dr. Dane Cook presented in our May SEC call, the response to exercise. The second paper assesses orthostatic intolerance using a tool called the NASA lean test. In latter stages of MCAM, all sites began using the 10-minute NASA lean test, a clinical tool brought to the group by Dr. Benjamin Natelson. He's been using this for decades. And in his hands, he includes a measurement called end Tidal CO<sub>2</sub> which allows for identifying reduced carbon dioxide levels in the blood.

Other papers in progress include one for cognition testing presented at the recent IACFS/ME meeting. One describing the differences among patients with ME/CFS at MCAM clinical sites, and one describing the association of natural killer cell function with other measures of ME/CFS illness. We continue to work on a paper reporting on the use of PROMIS measures of sleep and pain to describe the experiences of people living with ME/CFS. We expect to have at least three of these manuscripts published next year.

We also continue to add new content to our website. There are ongoing efforts to provide more Spanish translation to our existing content. In August we posted our Patient and Healthcare Provider toolkits for both ME/CFS and Post COVID-19 Conditions in Spanish.

The voice of the patient segment featured on our website continues to grow with first-hand accounts of the disease from people living with

ME/CFS. Our most recent post is from the perspective of a mother and son both living with ME/CFS. Over the past three years, the voice of the patient segment has garnered nearly 300,000 webpage views. We're working on a new post which should be posted by the end of the year.

Finally, I'd like to update you on the report of the systematic review of evidence related to the management of ME/CFS. As you likely remember, we undertook the systematic review as the first step in what we hoped would lead to the development of comprehensive ME/CFS treatment guidelines. We are committed to advancing the research and supporting the ME/CFS community. However, we recognize that the systematic review did not provide enough evidence to move forward with treatment recommendations at this time. So, despite the fact that improving clinical care remains a critical issue, we feel it is in the best interests to not proceed. In the interest of transparency, we will be posting the final report, comments received, and responses to these comments on our ME/CFS website. We will not be publishing the systematic review in a peer reviewed journal. I want to note that with the posting of the systematic review, we're not endorsing specific studies. But we do want the information to be available should others in the ME/CFS field undertake a review of the literature in the future. We continue to provide other resources that clinicians can refer to such as a link to the ME/CFS clinician coalition website and the IACFS primer. We will also be adding a link to the United Kingdom National Institute for health and Care Excellence or NICE guidelines that were published the end of October 2021.

Now I would like to introduce our guest speaker, Dr. Hector Bonilla. Dr. Bonilla is a Clinical Associate Professor of Infectious Diseases with Stanford University Medical Center. Dr. Bonilla received his medical degree from the Universidad del Valle School of Medicine in Cali, Colombia. After completing his residency at Sinai Hospital of Detroit, he moved to the University of Michigan where he completed a fellowship in infectious diseases. He spent much of his career in clinical management of HIV and AIDS and hepatitis C at Louisiana State University. In 2018 he received a Ramsay award from Solve ME/CFS Initiative for his work on a genetics project encompassing ME/CFS and the herpes virus. Welcome, Dr. Bonilla.

Dr. Hector Bonilla: Can I share my screen? Okay. Got it. Okay. Thank you for the organizers of this meeting for inviting me here to share my experience in working in post-COVID. I'm going to divide this kind of presentation in different

sections, the first section is definitions of diagnosis of chronic fatigue syndrome as well as post-COVID syndromes. The second section is going to be chronic fatigue syndrome and post-COVID area. The last section is what we learned from both, from ME Chronic Fatigue Syndrome ME/CFS and what we learned from a post-COVID ME/CFS.

Next slide. So, I have no conflict of interest.

Next. So, on the definition of chronic fatigue syndrome have been based on a cluster of symptoms. I have involved over time. There is no biomarker or blood test can define as chronic fatigue syndrome. The definition is based on symptoms put together helping them find this illness. In 1994 the CDC pulled the Fukuda criteria and based the most important definition is severe and profound fatigue. After being explored all possible causes of fatigue and the symptoms of fatigue have been persistent for longer than six months. Other criteria like Canadian consensus criteria emerged in 2010. In this kind of criteria, they outlined a post exertional malaise or PEM or “crashes” as well as pain and the symptoms persistent for longer than six months. The more recent criteria for chronic fatigue syndrome came from IOM in 2015. Next slide, please.

So, in this kind of criteria, they proposed five main symptoms, the first one three are essential and one or both of them could be considered for make a diagnosis of chronic fatigue syndrome. The first is the fatigue. The fatigue had to very specific characteristic, it had to be onset severe incapacitated fatigue that interfered with a person's personal, social, educational, and professional life and fatigue that lasts longer than six months is not alleviated by rest and is not related with overdoing too much exercise.

The second criteria is post exertional malaise or crashes they allow the patient to experience after physical activity stress or too much overstimulation and exacerbation of symptoms and sometimes could be delay in presentation. The unrefreshing sleep are people after having a night long hours of sleeping they get up exhausted and sometimes these symptoms could be very incapacitating for patients, worse part of the day could be when they're waking up.

There are two additional symptoms cognitive impairment, people call brain fog, that includes problems with cognition, memory, concentration, process information, and the orthostatic intolerance that could be an indicator of autonomic dysfunctions in those patients.

So, ah, the burden of this illness affects 836,000 to 2.5 million of the American population. Mainly are females, age of onset is 33 years old and range from 10 to 77 years old. Symptoms can persist for years or even decades in some patients, and the economic impact has been estimated 18 to 24 billion dollars. So the impact on society is humongous.

Next. So for long COVID definition had been no consensus about it but different institutes have different kind of definitions. Here we have the CDC who define long COVID as people who have symptoms longer than 28 days since first symptoms appeared. The UK, the National Institute for health and Care Excellence define symptomatic COVID symptom from 4 to 12 weeks and post-COVID syndrome defined basically symptoms longer than 12 weeks. And WHO reached a consensus in October of this year, they established the new criteria for definition of long COVID, and they define people who have symptoms longer than three months and last for two months and cannot be explained by any alternative diagnosis. Like you see here, the prevalence of post-COVID syndrome depends on which criteria you use, if you're the CDC, could be maybe longer, if you're the WHO you could see the prevalence of this illness to be lower. Next.

So, most chronic fatigue patients they refer to having an initial presentation of other illness. Also, most of the data have been retrospective data, no prospective data to follow up those patients and see what happened. Having COVID gives you an opportunity to establish the link between a viral infection and chronic fatigue syndrome. Here I want to present a couple cases from my clinic who referred initial infection follow chronic fatigue syndrome. The first one is 39 years old female. She's working as an executive assistant, she physically very active. She bikes over the weekend 30 to 40 miles. She's very fit, no medical conditions except anemia, she's treated by her primary care physician with iron pills. In May 2017 she developed this rash that's classic for herpes zoster. And three weeks later after this rash, she started experiencing sore throat, severe incapacitating fatigue and lymphadenopathy in the cervical area and she went to see her primary care physician who diagnosed her with mononucleosis EBV. When the Monospot test came back positive, EBV-VCA IgG, IgM came back positive, and the ALT/AST test elevated 10 to 20 times normal values. She was diagnosed with acute mononucleosis infection, mononucleosis EBV. She was treated by her primary care physician with Valacyclovir. She recovered from this infection but after infection she have persistent incapacitating fatigue, brain fog or cognitive dysfunction, interfered with her work, she has post exertional malaise, unrefreshing sleep, myalgia,

neuropathic pain. She came to Stanford to the clinic and was given the diagnosis of chronic fatigue syndrome.

Next. The next patient is 37-year-old female who in December 2017 she went for a vacation in Cabo San Lucas and she presented a few days after her vacation with severe diarrhea, myalgia, fatigue, low grade fever, and a diffuse rash. Her labs show leukopenia and neutropenia. And here we see on the left this very fine rash that is classic for Dengue. Initial test came back negative but PCR for Zika came back positive. Later a sample was sent to CDC in Fort Collins for testing arbovirus and came back positive for IgM for both Zika and Dengue virus. For two years post-infection she continued experiencing severe fatigue, post-exertional malaise, OI and brain fog. She used to hike around 20 miles in a single day but now she can walk between 50 feet, and the maximum she can do is two miles one or two times a week. She came to Stanford and we confirm the diagnosis with chronic fatigue syndrome.

So we here in these two different cases we represent two different kinds of viruses, one that includes the herpes virus that includes herpes zoster EBV and the second one is the arbovirus, Dengue and Zika virus and they're a family of viruses that lead to chronic fatigue syndrome. Next.

So when you are looking for in the last decade there have been report clusters of patients with chronic fatigue syndrome. In 1934 in Los Angeles in 1948 in Iceland, they call Iceland disease, and from there many outbreaks in the UK and Europe, Boston area, Miami, South Africa, and Australia. So these kinds of clusters of patients with chronic fatigue syndrome implies could be an environmental factor or maybe an infections as a potential cause of these kind of problem. Next.

So, in Stanford to address the issue of post COVID condition we created a post-COVID clinic, like many centers in the country and we function based on internal medicine and infection disease. We have patients who have diagnosis with COVID and have symptoms longer than four weeks. Those patients had been evaluated in the clinic by infectious diseases or internal medicine and according to the findings and symptoms can be referred to the multi-disciplinary groups and it could be chronic fatigue clinic, pulmonology, cardiology, autonomic, neurology, psychiatry, rheumatology. Depends what they have and depends on feedback to the hub with patient follow-up every three months in connection with the primary care physician. Maybe those patients had part of different trials as well as part of the COVID trials. Next.

So in Stanford we look at the data a couple weeks ago on 109 patients diagnosed with PACS. The criteria we use to see patients in the clinic, need to have clinical symptoms of COVID, test positive for COVID that can include the PCR, antigens or anti bodies before any vaccination. We evaluate those patients on 29 symptoms and grade symptoms on a scale of 1 to 5 Likert scale with 1 represent patient with mild illness and 5 with mild symptoms. And we evaluate the risk factors with severe COVID that include chronic pulmonary disease, chronic heart disease, liver, cirrhosis, renal failure, patient immunocompromise, obesity and others. And we evaluate in those patients the functional status in a scale 1 to 5 with 1 include patient have no symptoms and 5 people with severe incapacitated. Next.

So, for this kind of cohort 109 patients, COVID patients, we exclude 15 for many reasons. Many of them have diagnosis of chronic fatigue syndrome. Many of them have no diagnosis test in the chart or patient have other conditions that can explain their symptoms. So, we end up with 94 patients and here on the right, the table on the right I present the data from these 94 patients and what kind of characteristics we see. We see the mean age is 46, the mean days of follow up is 280 days. Patient majority were females. White population predominantly in 61 percent of the patients. The majority of patients, 86 percent have diagnosis of COVID based on PCR results. And interesting 80 percent of the patient who had post-COVID symptoms were not in the hospital they had either mild to moderate COVID disease. That surprised me because we have a tendency to see people who have been sick in the hospital have more post-COVID symptoms than the people with a mild or moderate disease and we're the opposite. Another thing, most of the patients was treated as an outpatient. Over 50 percent of the population have no comorbidity, they are healthy populations. The majority of people at the initial presentation have severe symptoms. Next.

So, we decided to with this kind of cohort to address how many of those people fit into the chronic fatigue syndrome clinical criteria. So, we select patient who have symptom for longer than 180 days, so six months of infection. In the Likert scale, the fatigue and symptoms to be a Scale 4 or greater, try to compare the severe fatigue, and functional status, a grade of 3 implying people have some limitations in the daily activities of their life.

So, we use the IOM criteria as criteria for diagnosis of chronic fatigue syndrome. Next.

So when you described the criteria and we select the patient for the study and drove from 94 to 70 patients that we want to include in the analysis here. Interesting in this kind of population 70 patients that included in our study based on this criteria, 56 percent fit into the IOM clinical criteria for chronic fatigue syndrome. When we're looking for this population in more details, there's no difference in the age, sex probably like we see in chronic fatigue patients is more female population, more Caucasians, white population, and majority of the patients, over 80 percent, had been a mild or moderate COVID infections. We had just one patient from this cohort that had been in ICU that have no chronic fatigue syndrome. Majority of people were healthy without any comorbidities. 74% of the patients fit in all the five criteria for the IOM criteria. And 26% had four of the five symptoms. Next

So the question is what we learned so far for chronic fatigue syndrome. This is not COVID. What we learned from before COVID. We know in this population have abnormality in cytokines, low NK cell function. There're evidence of brain inflammation but different neurology like on PET MRI or Magnetic Resonance Spectroscopy and evidence of mitochondria dysfunction. Next.

So, the two biggest studies in cytokines came from a group of Landi, 34 cytokines in 100 patients with chronic fatigue syndrome versus 79 controls. They found significant low levels of IL-16, IL-7, VEGF-A alpha, and CX3CL1, MIG, and CXCL9, and increased level of CCL24. Montoya, three years ago he published one of the biggest study of cytokines in patients with chronic fatigue. He measured 51 cytokines in 192 patients, almost double the population in the Canadian group, and 392 controls. He found out 17 of the 51 cytokines are higher in the chronic fatigue population, and the levels correlate with severity of the illness. He found out their Resistin was low level and TGF- $\beta$  was elevated in this kind of population. Next.

So, the studies, it's not consistent. Bigger studies but the cytokines are different. I think for me had to do with – they are cross-sectional studies. So at one point when you look at this data on more longitudinal way, a small study of 10 patients with chronic fatigue and 10 controls and he draw blood daily for 25 days and looking at 51 cytokines, and one of the cytokines he was focus was Leptin. We see Leptin in green. We see Leptin some days are up and some days are down. But when you ask the patient can you plot the fatigue symptoms, and he found a stress correlation between Leptin levels or cytokine levels and the fatigue symptoms. We

can conclude the cytokines directly or indirectly are the driver of symptoms in patients with chronic fatigue. Next.

So, NK cell function is something that had been already been report decreasing in patients with chronic fatigue. So here we have a study we did in Stanford on 234 patients, 102 controls, 132 patients with chronic fatigue. The chronic fatigue was defined based on the Fukuda and IOM criteria and majority of patients were females, and we have the NK cell function measured based on the lytic activity. Here in the white we have the levels of lytic activity. In the X we have the different concentration in NK cells and the lytic activity. Here we see in orange the control patient and in blue the patient with chronic fatigue. We see in the chronic fatigue population lower NK cell function compared with the controls. Next.

The brain image has been able to show in patients with chronic fatigue areas of decrease in white matter here in these images from Stanford we see normal patients white matter compared with in the lower portion the white matter is lower, with enlarged ventricles in patients with chronic fatigue compared with normal controls. Next.

To evaluate inflammation, there is a way to measure by the amount of TSPO in the brain. And TSPO had been considered a biomarker of microglial cell activation. So, this TSPO is a protein expressed in the outer membrane of the mitochondrial. It is present in low level normal or healthy brains. And overexpressed in persons in neuro degenerative diseases and inflammatory diseases. It's a marker of glial cell activation, inflammatory responses, and oxidative stress, mitochondria homeostasis. Here I tried to bring the mitochondrial for biology, they have the outer membrane and inner membrane. The inner membrane space loading of protein is very important to maintain the differential electrons to transport and we have the makers with all of this. So here in the outer membrane this protein on the right is a protein that attach class trail and then correlate with inflammation. Next.

So when you do these kind of studies -- next -- and try to tag these kind of proteins, this we use, next, we use the carbon levels as a tracer or tag called DPA-713 PET scan. We compare the female 39 year old female compared with a healthy control 37 years is what we see in the brains of these patients. Next.

We see the difference here in yellow and red and the cortical area we see gray uptake with this tracer compared with a healthy control. It's an

indicator like I said of inflammatory responses going on in these kind of populations. Next.

So when you looking for the areas of the brain we see this kind of places increased is not all areas of the brain, mostly in the white matter so there is no difference in healthy controls as well as the patient with chronic fatigue, but we see in chronic fatigue population there are specific areas of the brain, brainstem, thalamus, hippocampus, amygdala, and pons, with higher uptake compare with healthy controls. Next.

So there's another group from Japan, from Osaka, they use the same kind of technique but trace a marker for TSPO, they use PK11195 and they look at the brain and they found out again in people with chronic fatigue they have a higher TSPO, higher NCSO neuro inflammation. Here we have in blue the healthy control. In pink we have patients with a chronic fatigue that's higher, the tracer, and they find a physical relation between the tracer and symptoms of the patient. The cognitive dysfunction, the pressure and pain. So the higher the threshold, the higher the symptoms in these kind of patients. Next.

Again the areas in the Japan group is identical the areas that we find in Stanford are taking in persons with in chronic fatigue, midbrain, pons, thalamus, cingulate, Amygdala, hippocampus. When we try to analyze the functions in those areas we see explain the majority of symptoms that the patients experience. For example, the area of the thalamus is people experience pain, the pons and midbrain, area of the autonomic system or the autonomic dysfunction in those areas, and in the Amygdala and hippocampus have to do with memory and emotions that explains the brain fog happening in these kind of populations. Next.

Other studies trying to looking for other areas of inflammation they used the whole brain magnetic resonance spectroscopy. There its study compared 15 females, 15 matched healthy controls, and they look at the different metabolites, choline, (MI) lactate and N-Acetyl-L-aspartate. And choline is a biomarker for inflammation. They found in patients with chronic fatigue increase the relation between choline and creatinine as indicated on the inflammation. Next.

So the other things we learned for the chronic fatigue population is changes in mitochondria functions. So in this study they evaluated mitochondria function in 35 patients controls without chronic fatigue, 52 with chronic fatigue and they found different mitochondria function, basal respiration, ATP production, proton leak, maximal respiration,

reserve capacity, decrease in this type of patient. Here on the right side we compare in the first two to the left are the fresh samples and the last two on the right compared the frozen samples. Focusing on the fresh samples we see here in the first square here in the right is the patient with chronic fatigue and to the left the healthy controls. In all patients with chronic fatigue they found decrease in basal respiration, decrease in the ATP production, decrease in proton leak, and decrease in maximal respiration and decrease in reserve capacity of those kind of patients. So, it's evidence those people have a mitochondria dysfunction. What is the driver of this is not clear, possibly related inflammation with an infection that target or attack the mitochondria. Next.

So, the thing is, what lessons we learned from now in post-COVID area? They're still in research that need to be clarified. Most of the data we have is based on what happened in acute phases. In post-COVID area, still information is common, hopefully in the next few weeks we can get better understanding. We see in people with post-COVID again the cytokines are normal, NK cells are normal especially in the acute phase. Areas of no inflammation and areas of mitochondria dysfunction, again this, more in the acute phase, no in the post-COVID area. Next.

So if you refresh the memory about in acute COVID we have three stages, first is viral phase, high viral replication, followed by inflammatory phase in pink, and we saw stage three more inflammatory. There are two big studies, one from Mount Sinai Health System that include 1400 patients who have been in the hospital for COVID and they look at cytokines and they found people have IL6, IL8, and TNF alpha have been correlated with poor outcomes. There's more recent study looking at effect TGF beta of cytokines have been associated with severe COVID-19 that have been in Montoya's paper, that have been elevated with people in chronic fatigue, TGF- $\beta$ . So how TGF- $\beta$  they have been correlated with NK cell function and the NK cells are very, very important in try to eliminate the virus. So still what happen in the post-COVID area six months after COVID, maybe two according to the WHO or 12 weeks according to the UK criteria or 28 days after CDC, this area is still in research very active. Hopefully in the next few weeks we can get more information. Next.

So this paper came from Singapore. They are following people a longer time and they looking for cytokines, persistent inflammation. They follow this patient for 180 days and they have 101 patients with COVID test positive by PCR and they have 38 patients with mild symptoms 34 with moderate, 29 with severe, and 24 healthy controls. In this one would

represent in those graphics we have in these kind of dots interruption correspond to healthy controls and the different colors, we have the green is mild disease, blue is moderate disease, and kind of burgundy is severe disease. In all groups they see a persistent inflammation, elevation of the cytokines even 180 days after the infections. Interesting, when we compare the cytokines, for example, the MIP-1 $\beta$ , VGF-Alpha, VEGF-Delta there are some cytokines have to do with vascular repairs. As one of them they hypothesized in patients with post-COVID in like uh the micro circulation possible thrombosis or [indecipherable] that can lead into blood flow dysfunction and lead into more inflammatory responses and possibly explain most of the symptoms. This all persistent based on inflammation by IL-17A, IL-12, and IL-1 $\beta$ . Next.

There's another study looking for the brain study here in Stanford by Tony Wyss-Coray. We had eight patients who had COVID who died. They have the brain compared with 14 patients as a control. They found in those brain they have increase of the vascular macrophages, T cells, and micro glial cells. Here we have in the right upper part here in kind of blue color there are increase in the first one of the perivascular macrophages, in the second a panel increase in the T cells, and the last one micro glial cells compared with the control populations. We're looking for in the brain the cells have been more activated glial cells, and this upregulation of gene IFITM3 have been expressed in the choroid and in glial cells and this kind of gene activation is corresponding with potential infection. However, when they're looking for a PCR in the brain tissue they didn't find it. But there is brain inflammation. Here we have and we see on the left side in the lower part normal brain and right side has patient with COVID that shows increasing micro glial cells and immuno-inflammation. Next.

Again, so this is this is in acute COVID they're looking for mitochondrial dysfunction in patients: 9 healthy controls, 7 with COVID-19, and 7 people who have a pulmonary infection, not COVID). Again they see basal respirations, ATP link, maximal respiration and reserve capacity and the wide decrease in patients with COVID compared with healthy controls. Again, this data need to be evaluated in patients with prolonged COVID and see if his mitochondrial dysfunction remain but this area need to be explored in more detail. Next.

So in conclusion, we find out the chronic fatigue and chronic fatigue post-COVID they have similar clinical presentations. Most of the post-COVID-19 patients they are more in white population, healthy individuals, with

mild to moderate COVID-19 infections. Both groups, the chronic fatigue and the chronic fatigue plus COVID-19 are characterized for decrease of cytokines, low NK cell function present in chronic fatigue, and acute COVID have been correlated with poor outcome. This area is under inflammation in chronic fatigue syndrome and will last in the post-COVID symptoms and this needs to be evaluated at multicentric sites and include larger population to see if those kind of findings are persistent.

I will open here for questions.

Christine Pearson: Thanks so much, Dr. Bonilla. That was excellent. Can you hear me? Yes. Okay. So everyone now we'll move on to the Q&A section. This may seem like overkill, but we have four ways that you can ask a question to make it easiest for everybody to do whatever you're comfortable with. If you're joining us on the Zoom, the easiest way to show that you'd like to ask question, click on the raise hand button under the webinar controls at the bottom of your screen or if you prefer you could type it into the chat box, and it will be sent to the CDC team manager on call. I will say if everybody floods the chat it's sometimes hard for us to see all of them so it may take us a little longer to get to your question. If you're joining by phone, you can enter star 9 on your phone to join the question cue and when it's your turn you press star 6 to unmute yourself. Lastly, we have the ME/CFS email address which is [mecfssec@cdc.gov](mailto:mecfssec@cdc.gov). Again that, will be the slowest option. So I hope that helps. While folks are getting a chance to raise their hands, we did get a couple of questions that came in during it that I thought we could start with just to sort of give some time for that. First as I'm paraphrasing here because we've got several people who asked the same question. The first one is in referring to the COVID UPP and COVID RELIEF studies, what criteria will be used to identify ME/CFS patients in these studies and will it include PEM and/or are we in discussion with others at CDC in terms of the criteria for other long COVID studies that are not through the program here?

Dr. Elizabeth Unger: So for the first part of the question, CDC is using the Institute of Medicine clinical diagnosis so PEM is part of the diagnosis. We will be characterizing as many of the components of the illness as possible. Many times using the instruments that we have data on in MCAM. We are not involved in every study involving post-COVID conditions conducted at CDC but we are part of the post-COVID conditions team and we have given input on quite a few studies and the idea is that there will not be a requirement per se but post-COVID conditions -- sorry, post-exertional malaise is one of the symptoms that we ask everyone a

question about so we can get data to understand it. Sorry. When I move.  
The light.

Christine Pearson: We'll be very environmentally conscious here at CDC.

Dr. Elizabeth Unger: That's right.

Christine Pearson: One more quick one which was it wasn't clear whether this was for Dr. Bonilla or Unger, if you'd like to um, if you'd like to each answer quickly that'd be great, which is asking whether we are we doing collaboration with Bruce Patterson on these studies?

Dr. Elizabeth Unger: We are not at CDC right now.

Dr. Hector Bonilla: I am not.

Christine Pearson: Okay. All right. So I did forget, I'll go to the raised hands and other piece now and again we'll try to get to as many as we can. Please try to keep your questions as succinct as possible so we can try to get as many people as possible. Okay. So we will turn that over now -- the first question we have is from Michelle Lee if you would like to go ahead and speak.

Michelle Lee: Can you hear me?

Christine Pearson: Yes.

Michelle Lee: All right. I'll try to be succinct. I guess my question is to Dr. Unger. I'm an analyst and researcher and as somebody who struggled and I think failed to come up with particularly good survey instruments in my own area of research, what strikes me about this field that seems to be now a problem also with the post-COVID evaluations is a chicken and egg problem. You have ...how you identify something which you haven't fully elaborated on in a very granular way which can be easily accessed by clinicians who are incredibly busy and now under incredible stress and they're not going to be going and doing research and looking at all these wonderful studies, right? I guess part of the solution might be fixing the coding problem, but that's only part of the solution. So I'm just throwing that up as a, you know, problem that I see. Also emerging in the post-COVID field.

Dr. Elizabeth Unger: Yes, I will ask Dr. Bonilla to comment as well based on his experience as a clinician. The syndromic illnesses like ME/CFS are very challenging for healthcare providers because there's not a simple test and it requires a lot of medical expertise to put the symptoms in the right context. What's important about the case definition in particular the IOM report, we give

tools to clinician of how to get a good medical history that will allow them to consider ME/CFS and explore what the nature of the patient's fatigue is and what brings it on. As far as the instruments that are being used, there was a common data element initiative for ME/CFS. We realize that we are continuing to work on that. Also common data elements being developed for the post-COVID conditions field as well. We hope that many of the same instruments will be used in both and we're particularly optimistic about the PROMIS instruments that were developed by NIH. But yes, we agree, this is a problem. Dr. Bonilla can you comment on a clinician what your challenges are?

Dr. Hector Bonilla: My challenge at the beginning when we open the clinic was how we think we're going to evaluate for those patients how we can collect data because we want to see patients and able to get this information. The reason we get to customize evaluation, we did 29 symptoms that have been reported in those patients and tried to operate in base of severity. In this one decide how to evaluate about the clinical status of the patient from no symptomatic to severe incapacitated and tried to use the same kind of standard for all of our patients. So those kind of criteria help us at least to quantify in more objective way every single patient data for analysis. The reason I was able to come out with this kind of information I just shared with you, I was able to figure out for me with this kind of tools we use we find out something that surprise to me. I expected initially people with severe COVID have more chance of post-COVID and quite the opposite. We see people with mild and moderate disease have more post-COVID symptoms than the people without. I think we are learning in a way and try to see what kind of tests perform better or not. We start using now in my population I'm using in my clinic in my chronic fatigue population, MFI scores as a symptom for severity in this kind of population, I still don't have enough data but is this data is going to show? Let's see. I think we need to extrapolate those conditions to try to apply in patients with post-COVID and see how we can validate. It's something we struggle and see what the best way assess those patients and follow up long-term.

Dr. Elizabeth Unger: I would like to answer one more thing before we go to the next question. That is, ME/CFS is very heterogenous and patients are very heterogenous. And the patients with post-COVID conditions are very heterogenous, very complex medical conditions. Part of that is the reason why the characterization of all the symptoms is really, really important right now. Instruments that allow capturing both the frequency and severity of the wide range of symptoms that these patients are

experiencing is going to be important for us to divide out the phenotypes into subgroups that may be present.

Christine Pearson: All right. Great, thank you. As you see me looking down, I'm looking really strange, I'm trying to keep up with the chat and the other things. The next question, Billy Hanlon.

Billy Hanlon: Yes, hi can you hear me? My question as I posed in the chat, when will CDC convene a meeting of ME/CFS stakeholders to give input in how the evidence review comments and responses can be put into an appropriate context on the CDC website?

Dr. Elizabeth Unger: Thank you. That's a good question. We had not planned to have -- to convene a meeting specifically on this topic. I think we have received a lot of feedback but your suggestion to elicit more is something we will consider. Thank you.

Christine Pearson: Next to Art Mirin.

Art Mirin: Does CDC endorse the flawed conclusion of the EPC evidence review that there is evidence that GET and CBT have moderate benefit for people with ME/CFS versus inactive controls and that there is evidence that GET is safe for people with ME/CFS? I ask this because this was not the conclusion of either the NICE evidence review or the NICE treatment guidelines. Thank you.

Dr. Elizabeth Unger: Thank you. The systemic review does not come out and say that GET is safe or effective. It indicates the quality of evidence is very, very limited and it does include the caveats of using the appropriate case definition.

Christine Pearson: Next to -- I don't have a name. The area code is 646. The ending of the phone number is 125.

Are you here? You can press star 6 to unmute yourself. The wonders of technology. We'll give you a second more to try to do that and go on to the next question which came in on the chat.

Caller: Hello.

Christine Pearson: Oh, yes. Good.

Caller: Was someone trying to let me ask a question?

Christine Pearson: Yes. Go ahead.

Caller: Okay. High. This is Eileen Holderman. I'm an advocate for ME. Thank you for the call

and the presentation. My question is about ICD-10CM. It's been a big, big issue concerning how ME affects SEID and even COVID-19 long haulers are classified in the ICD-10CM and we have a proposal out by NCHS as well as 7 organizations but they are very much contested and a lot of advocates, independents and organizations have opposed those for the very reason we don't believe that those diseases or disorders are the same. What is the official position, Dr. Unger, of CDC whether or not ME/CFS [or SEID] and COVID-19 long haulers, why is there a push to put all these together under a single classification when they're entirely different? Thank you.

Dr. Elizabeth Unger: Okay well. I it's my understanding, is there is a separate code for post-COVID conditions that just got introduced in October. We're also aware of a proposal for changing the ICD-10CM code for ME/CFS that has been submitted by a number of advocates that NCHS is considering. They shared this with us and we are reviewing it and it seems, you know, we're in the process of developing a response to it. But it seems very reasonable to us. So I don't think they're coded as the same thing. We don't yet know for sure they're the same thing. We think they're related. I honestly look forward to the day when we are not calling these syndromes but can divide them up into the pathogenesis that's involved. Until we have that, we have these descriptive ICD-10 codes.

Christine Pearson: Thank you. For those who may not be aware, that's NCHS is the National Center for Health Statistics which is here at CDC, that's the group that's in charge of coding issues. We're going to toggle over now to the chat function so I have a question here that says: Dr. Bonilla, for those suffering from CFS and unable to participate in these long COVID studies, would you recommend supplements -- why is it not letting me -- would you recommend supplements that -- oh, now I can't read it I'm sorry. Okay. Go ahead and start talking.

Dr. Hector Bonilla: I think first of all there's no standardized therapy either for chronic fatigue syndrome, before COVID and post-COVID. So the values of the supplements have not been validated. Everything's going to be off label. Whatever I'm going to say is gonna be my personal opinion. I do not say opinion from the CDC or IDSA or Stanford University but I think the best supplement that people can have is a good diet because all the supplements you need is in the diet. For me, my personal opinion again, the supplements are not benefit for the patients, maybe the manufacturer of the supplements, yes. This kind of area have been booming across the nation. Every single corner we have a place to sell supplements and it's good business for these kind of patients. I kind of

tell my patients if you want to supplement, get good nutrition, get high quality food, high quality of fruit vegetables. There's some evidence that some foods can lead to more inflammation or less inflammation. There's data about possible carbs and sugars can lead to inflammatory responses and Omega-3 or goods have been linked with decreased inflammation so plenty of data about this one. A more recently a paper came out from Stanford looking for cytokines and microbiome and diet and they found possible fragmented diet has benefit in patients with chronic fatigue. This is my intake about supplements and many of my patients spend a fortune in buying supplements that I think have no benefit to them. Again, this is my personal opinion, it's not opinion from CDC, IDSA, or Stanford.

Christine Pearson: All right. Excellent. Thank you. Sorry about that, questioner. It just would not let me scroll. So we've got one more in the chat which says what's being done to study term ME/CFS patients who may hold the key to new ME/CFS patients as well as long COVID patients?

Dr. Hector Bonilla: I'm kind of confused this question. Could you repeat the question again because I couldn't understand the question.

Christine Pearson: Sure I think it actually may be for Beth. It doesn't say who it's for. It says what is being done to study -- no, to study termed ME/CFS patients who may well hold the key to helping both new ME/CFS patients as well as long COVID? I think that's meaning long-term COVID. Long-term ME/CFS patients related to long COVID patients and how it relates and other new ME/CFS patients.

Dr. Elizabeth Unger: Right. As Dr. Bonilla pointed out, the investigators of long COVID are really looking to the ME/CFS literature and pulling up everything. This literature has been established on long-term ME/CFS patients. So we'll be comparing the data that's present along with data that we're finding out in the long COVID patients that meet ME/CFS criteria. It is -- in our phenotyping study we're doing it in collaboration with a clinician that has a lot of expertise ME/CFS and has characterized patients with long-term ME/CFS so again we'll have a good basis for direct comparison of the patient characteristics as well as some of the biomarkers that the investigator is planning to do. I think what's interesting about the question is specifically focusing on long-term ME/CFS. We don't really know how the illness changes, but we do think again from the anecdotal experience from the patients that the experience of their illness changes or can change with time. It is possible that early onset ME/CFS is different from long-term ME/CFS. I would imagine, my imagination is that long-term ME/CFS would be more matched closer to the patients that are

presenting with long COVID just again because of the duration of illness and the symptoms could change over time. I think we have a lot of really good questions and a lot of attention now focused on this really, really important question. Dr. Bonilla, please comment as well because you're involved in these studies.

Christine Pearson: Dr. Bonilla, did you have anything you want to say about that?

Dr. Hector Bonilla: I think it's about the same question, I think different kind of my own perspective in persons with chronic fatigue syndrome is when they started the disease, the disease doesn't change, it waxes and wanes when the people overdo with crashes. But once it started, I see people with the same condition for decades. When I saw the disease 20 years ago, any changes, some days, I'm worse, sometimes better and go to the same baseline of chronic fatigue. So something established and I feel it's going to be -- people are persistent, I don't know for how long, is going to be similar thing that we see now in chronic fatigue patients could be the same thing we're going to see in post COVID. The two cases that I illustrated, I tend to present different cases with different viruses but leading to the same kind of condition. So it's something like many viruses that they can triggered this kind of immune responses and this persistent or this abnormal responses that lead into chronic fatigue syndrome. The study by Jarred Younger show the correlation between cytokines and fatigue syndrome is kind of interesting because they are about this kind of about -- it could be waxing and waning, it could be leading the symptoms of this kind of patients. Who is the driver of this kind of cytokine is not clear, possible a failing of the regulatory mechanism of how to control inflammation and immune responses is one possibility. Maybe some virus particles in the body and that could be activated as immune response is possible. So it's an area that's still in active investigation. We don't have clear answers. But time is going to tell and we have a great opportunity that COVID -- COVID was a blessing for chronic fatigue syndrome because we know about infection in people with similar symptoms and we are able to follow up prospectively with those patients and try to identify any potential biomarker that can predict what populations going into chronic fatigue syndrome and which ones they don't. We can identify maybe a genetics marker because we see more in females than males. Here in Stanford majority of the population I see is white population, maybe because of the area, could be a factor, but it's something like see that in the study I present to you, majority of the people were white. So there are areas still very in research, for example, for me my study and we ask the question why see

more post COVID symptoms in patients with mild to moderate disease. I don't see many people have been in ICU in the hospital. So it's not clear to me but possibly have to do with immune responses. We know in people with mild COVID they have a low antibody response the duration is shorter compared with people with severe COVID and they been in the hospital in ICU on the vent, they have high antibodies and duration is longer. Maybe those people have antibodies able to neutralize viral particles and less COVID. We don't know. But I think this kind of research is going to give you keys to understand this kind of chronic fatigue syndrome or post-viral syndromes more clearly. I think we make a terrible mistake to call it chronic fatigue because people start thinking those people are lazy and don't want to work but that's not the case. I blame the physicians who give it names and they want to corrupt this illness and they do not try to advance and understand what happen with these patients. When you see the patients suffering, I get angry with myself, I angry with my colleagues, why we did these things wrong from the beginning and instead to paying attention and try to read the issues that the patient have every single day.

Christine Pearson: Thank you. So, a few more questions. We'll go to Denise next.

Denise: Hello. Dr. Unger was recently quoted as saying that the Social Security Administration is doing its quote due diligence in gathering information from all sources to be prepared end quote with regards to the significantly increased numbers of patients with ME as a result of acute COVID-19. What are the data sources that CDC is using to provide data to FSA, what symptoms are required in that data, and what definition is CDC using to compile this data?

Dr. Elizabeth Unger: We have not provided exact data or numbers to my knowledge to SSA. We've had conversations with SSA in interagency discussions about post-COVID conditions. For post-COVID conditions we're very much in a descriptive phase and we are characterizing all of the phases of the -- all of the facets of the illness and the -- at this point we have stuck with our four week time frame as a point to start looking at patients that have not recovered. We recognize that the time between 4 and 12 weeks many patients will still continue to recover slowly and at 12 weeks it kind of does tend to plateau out. The reason that we suggest starting at four weeks is that so that supportive care can be given if a patient is not on an appropriate trajectory to recovery. So, all of the discussions right now, rather than formal definitions that exclude or included patients, we are trying -- we are trying to be very descriptive and describe patients that

have -- that are not recovering from COVID in the way we anticipate. This allows for being sure that we understand all of the phenotypes of the problems patients would have from the direct organ damage that can come from SARS, from the problems that can come from any chronic serious illness such as post-ICU syndrome, to the very symptomatic debilitating problems that happen in the absence of test abnormalities. So there's a number of things that are going on in these patients.

Christine Pearson: Thanks, Dr. Unger. Next question comes from Ben. I'm not going to try to mangle your name. I'm sorry. Are you still here, Ben?

Ben: Hi. Can you hear me now?

Christine Pearson: Yes, I can. Thank you.

Ben: All right. Thank you. First off, I wanted to say a quick thank you. I know that CDC sent around the program updates before this call and that was very much appreciated as a person with ME to follow along. So, thank you for that and I hope that will be a continued change for SEC calls. That was an improvement. I'm going to read my question because I'm having cognitive troubles and that will be simpler. I want to clarify something that you said, Dr. Unger about the CDC not planning to publish the evidence review. My question is upon that has the CDC decided to allow Oregon Science and Health University PC to publish the review themselves if they want to. That's what happened with the previous review that was done for AHRQ. So, what you've stated in your program updates doesn't actually clarify for me whether we can expect the review to be published in an academic journal or not. I would note you told us ME Action in 2018 that CDC could have some say in whether CDC publish the review themselves so could you clarify that question.

Dr. Elizabeth Unger: We've had conversations with OHSU and the investigators that did the work on it and they understand that we do not want to have this submitted for peer review publication and that's their plan.

Christine Pearson: Next, Teresa, I'm not sure how you pronounce it. Doesn't look like it's unmuting. Hello.

Teresa: Hi. Sorry about that. Thanks so much, Dr. Unger for your program updates and Dr. Bonilla for your presentation. Dr. Unger, will the final findings of the EPC review align with the NICE review which concluded all the evidence from all the review GET studies was population indirect, that is not applicable or not generalizable to people with ME/CFS, or does the EPC review continue to misleadingly indicate that the GET evidence

base is applicable to people with ME/CFS, that is that GET treatments are moderately effective for people with ME/CFS as defined by CDC and by the better most updated case definitions?

Dr. Elizabeth Unger: Okay. So, in the details of the systematic review, they do break it down by case definition. It's clear in that section the limitations of the evidence. In a simplified description in the appendix or in the -- in one version of the abstract, it can be, some of these details can be missed. We're working on clarifying that, making it clearer that there is a difference depending on the population that you're looking at. But regardless of the data that's there -- regardless of the population, however you look at it, the evidence is not strong, and we agree with NIH that what is needed is treatment trials for ME/CFS patients that are appropriately powered and have validated end points. The field is desperately in need of that.

Christine Pearson: Thanks, Dr. Unger. We let the questions go a little bit longer this time because of the length of Dr. Bonilla's presentation but I think we have time for just one more question. The next person in line is Michelle. I don't have your last name. I apologize.

Michelle: Hi. Can you hear me?

Christine Pearson: Yes.

Michelle: Hi thank you, thank you guys for your time today. As someone who has recently progressed from mild to moderate ME this past calendar year because I was unaware that this is what I had in addition to a primary immunodeficiency. I have been pretty horrified by the state of affairs out there for folks with ME and the number of people that don't have access to a physician, let alone a specialist. What do you recommend for people out in the wilderness, probably not an easy one to answer, and does the CDC or other -- or another entity have maybe a consulting physician or something that a primary care could tap into? It's bad out there. People don't have anyone to turn to.

Dr. Hector Bonilla: Can I answer this. I concur with you. I think they get frustrated because one, many colleagues don't believe in this illness so try to find a provider willing to listen is very difficult. This condition hasn't been made to medical schools. Medical students have been not taught about chronic fatigue syndrome, one of the limitations. So lack in education. However, the CDC start putting a pilot study, I'm part of this pilot study, it's called ECHO program, that we are going to take a team of primary care physician who have patients with post-COVID syndromes and try to educate them about this illness, they present the cases and we can advise

them we compare with a control and see if it's beneficial. This study is beneficial and I hope it's going to be beneficial maybe can expand this program for many places in the whole country. I think the problem is the misinformation and lack of education by the primary care physicians and the medical school regarding this kind of problem. It's time to face it, it's time to do something about it. I agree with you. Out in the wild as people struggle with this illness have been mismanaged, dismissed, and it's something that break my heart to see patients in my clinic go through this kind of problems. I think COVID is going to bring new faces in the chronic fatigue area because many people are talking more about the problem. There is some research going on in post-COVID area and hopefully things will be changed and this problem will be taken more seriously.

Dr. Elizabeth Unger: Yeah. Thanks. The project that Dr. Bonilla mentioned is the one I also mentioned with the federally qualified health center. They're the primary contractors on this. We really went to the federally qualified health center because they're primary care centers, they deserve a disadvantaged population, and we want models of care that are accessible to this kind of population. We absolutely agree with you that much more needs to be done and it is terrible that patients don't have access to care. That's our number one request we have over and over again is how to find a clinician that knows about ME/CFS. That's why we've emphasized our medical education projects that we have and we have started to have sections and focus on the medical student education and so we think that the post-COVID condition just the sheer onslaught of patients and the fact that doctors will know their patients before they get ill and will be able to be more understanding of what the patients are going through will make a difference but it's going to take concerted effort of excellent clinicians like Dr. Bonilla along with the government to make a difference.

Christine Pearson: Excellent, thanks.

Dr. Elizabeth Unger: Sorry. Go ahead.

Christine Pearson: I just added to the chat there was a suggestion to put in there the clinician coalition website which may be useful for the last question there and also for a couple of others that were in the chat so you might want to check that out. All right. So that brings us to the end of today's call. Thanks so much, everybody, for joining us today and for your interest. We wish you health and strength as we head into the holidays and try to

finish up the year and into 2022. Thanks so much, everybody. Have a great day.