CDC's 21st ME/CFS Stakeholder Engagement and Communication (SEC) Call

May 17, 2023

3:00 p.m. ET

Christine Pearson: Good afternoon, everyone. Welcome to today's ME/CFS Stakeholder Engagement and Communication Call which we call S-E-C or "SEC." My name is Christine Pearson, and I'm the Associate Director for Communications in the division where the ME/CFS program is located within CDC.

As you may know, we host these S-E-C calls twice a year, as part of our regular outreach and communications activities to provide information for people with ME/CFS as well as their loved ones, clinicians, and anyone else interested in the disease.

Our goals during 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. Jennifer Cope, a medical officer with the CDC's Chronic Viral Diseases Branch. Then we'll turn it over to our guest speaker from Kaiser Permanente Division of Research at the Oakland Medical Center in California, Dr. Jacek Skarbinski.

After Dr. Skarbinski's presentation we'll have a Q&A session. During today's Q&A, you'll 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 this call is open to the public, so please consider that before sharing personal information. We're also recording this call. Please disconnect now if you have any concerns about recording. We'll post a transcript and video as soon as possible after the call is complete. If you'd like access to closed captioning, or to read along with the text of the program update, the links for both should be posted in the chat box.

Now we'll turn to over to Dr. Cope to start the program.

Dr. Jennifer Cope: All right. Thank you, Christine, for that introduction and welcome everybody to the 21st S-E-C Call. I would like to begin with recognizing the continued dedication of the many ME/CFS organizations and advocates that work to bring awareness to the serious long-term illness. As many of you know, we observed ME/CFS International Awareness Day last Friday on May 12th. A highlight of CDC's participation in ME/CFS Awareness Day this year was the lighting of the Visitor Center and Welcome Sign at CDC's main Atlanta campus in blue lights on Friday evening. And just a reminder with summer rapidly approaching the sun is setting as late as 8:30pm here in Atlanta and that's when the lights became most visible. And we arranged to have photos taken at that time which you can see here on the screen. CDC also marked

ME/CFS Awareness Day with new social media posts each day in the week leading up to May 12th, and a new CDC ME/CFS Awareness Day Features webpage which can be found at our ME/CFS web site which is www.cdc.gov/me-cfs and we'll put that link in the chat. This page has also been translated into Spanish.

On this new web page visitors will find recent program updates, including a summary of education and outreach activities, and information about ME/CFS and Post-COVID conditions also known as Long COVID. One important item we continue to highlight is the October 1st, 2022, release of the new ICD-10 codes, which now includes a code specific to ME/CFS.

To help observe ME/CFS Awareness Day and to continue to raise awareness of ME/CFS in children and adults, the ME/CFS program developed a new podcast that reviews pediatric ME/CFS and how it compares to ME/CFS in adults. Our medical officer, Dr. Nanda Issa discussed ME/CFS in children and younger people and shared the current resources for health care professionals and families. Dr. Issa also participated in a podcast with the staff from the Journal of School Nursing in February 2023 to share results from the first phase of our ongoing school-based active surveillance project. You can find links to both podcasts on our ME/CFS features page. Finally, in February 2023, we featured a Clinician Outreach and Communication Activity or COCA Call titled "Evaluating and supporting children in adolescence presenting with Post COVID Conditions. A link to this webinar can also be found on our website.

We also highlighted the collaboration with WebMD's Chief Medical Officer John Whyte who interviewed a person with ME/CFS and Dr. Valerie Montgomery Rice, President of Morehouse School of Medicine, as part of a series to describe findings of the general public's knowledge, attitudes, and beliefs about ME/CFS. These videos will be available to watch on WebMD's website until May 26th and we encourage you all to take a look.

CDC's ME/CFS program continues to strive to raise awareness of the disease through educational efforts and collaborations. I'll now provide updates on some of these activities. We continue to partner with the National Association of School Nurses to not only collect information about ME/CFS in school children, but also to educate school nurses about the disease. An overview of the School-Based Active Surveillance Project can be found on our website under the section called CDC's ME/CFS program. The first phase of the project was started in 2018 and completed in September 2021, and we shared preliminary stages of this work at the 2022 IACFS/ME conference, which was held online. The manuscript of the first phase was recently published in the April 2023 issue of the Journal of School Nursing. We are currently in phase two of the project which started in 2021 and will continue until 2024. In the second phase we continue to expand the work to additional states. The approval process for information collection was just completed this month and the school nurses are now entering the data collected from the 2022-2023 school year. Since the beginning of this project in 2018, seven courses have been developed to build school nurse capacity on the School-Based Active

Surveillance and ME/CFS. There have been over 33,000 people who have registered and downloaded these courses.

Meanwhile we've continued to publish findings from the multisite clinical assessment of ME/CFS, or MCAM study, for which data collection was completed in 2020. As of April 2023, there have been eight peer-reviewed publications from the MCAM study. These include publications describing the study protocol, assessing orthostatic intolerance, abnormalities, exercise testing, validating instruments to measure fatigue, sleep, and pain evaluating methods of extracting medication data and natural killer cell function testing methods. Previous S-E-C calls we mentioned that we were working on describing co-occurring medical conditions in people with ME/CFS. As a result, we submitted two abstracts to share these preliminary findings at the 2023 IACFS/ME conference, which will be held July 27-29, in Stony Brook, New York. One abstract assesses autonomic dysfunction in people with ME/CFS and the other abstract describes chronic overlapping pain conditions like fibromyalgia and irritable bowel syndrome in people with ME/CFS. We plan to use these analyses to help tailor our education materials for clinicians who manage care for people with ME/CFS and overlapping conditions. We are also in close communication with the NIH about linking MCAM biospecimens to the NIH's search tool, which is available to researchers. When the linkage has been completed, we plan to make the baseline clinical epidemiologic data collected for MCAM available through the map ME/CFS data portal. With the sharing of biospecimens and data from our MCAM study, we hope to generate more research interests and publications to advance ME/CFS research.

Now I'll provide updates on some of CDC's direct to healthcare professional educational activities. As of April 2023, we have partnered with Medscape to produce six online courses and one print supplement. Through the online courses we have reached almost 114,000 learners, 47,000 test takers, and issued about 38,000 course completion certificates. Five of these courses have reached the time limit for renewal of continued medical education or CME credits. However, the courses can still be viewed on the Medscape website. CDC is also sponsoring a new Medscape Spotlight CME course called "ME/CFS Diagnoses and Management in the Age of COVID: Expert Insights." The expert faculty participating include Drs. Anthony Komaroff and David Systrom from Harvard Medical School, and Dr. Lucinda Bateman from the Bateman Horne Center, an ME/CFS specialty clinic in Salt Lake City, Utah. We anticipate Medscape will launch this course at the end of the year.

Next, we'll turn our discussion about our work and plans regarding Post-COVID Conditions or Long COVID. As you know, the similarities between ME/CFS and Long COVID offer a unique opportunity to study and gain a better understanding of chronic conditions that begin after an infection. We are leveraging interest in study of Long COVID to raise awareness of ME/CFS and related conditions among members of the healthcare community. In particular, I'd like to highlight an expert commentary by our program that was recently published on the Medscape website. The article is titled, "Treating Long COVID Brain Fog with ME/CFS Guidelines." It

specifically focuses on brain fog, which has long been a symptom with people with ME/CFS. In the article we discuss 5 things to know about management of brain fog in ME/CFS, and how this experience can be applied to treat cognitive symptoms in people with Long COVID. In addition, early findings from several of our Long COVID projects will be presented at the IACFS/ME conference this year.

One project, COVID-UPP, which stands for COVID, Understanding the Post-Viral Phase, is a study based in southern Florida among adults. This project focuses on Hispanic or Latino people who tested positive for the virus that causes COVID-19 and still had symptoms more than three months after their COVID infection. A group of patients who fully recovered from COVID-19 is also included as a control. The study uses surveys to assess participants' health over time. A subset of participants will have an in-depth physical, cognitive, and medical tests to further characterize their illness. As these same tests have been performed on people with ME/CFS in previous research, the investigators plan to use the information gathered during this project to better describe similarities and differences between Long COVID and ME/CFS.

Our program will present two abstracts from the study at the conference this summer. The first will describe symptoms in people with Long COVID and is titled "Impairments in cognitive, physical and social functioning among people with Long COVID," and the second will focus on post-exertional malaise in people with Long COVID.

Another Long COVID project, the Multi-site Study of Post-COVID Conditions (or MPCC), collected health data from medical charts to describe the health and medical care of patients at clinics designed for post-COVID care. This project will help classify the types of post-COVID health problems and care needed, as well as describe the healthcare patients received in these dedicated post-COVID clinics. An abstract from this study that focuses on ME/CFS like illness among patients in three post-COVID clinics was accepted for an oral presentation at the IACFS/ME conference and a manuscript is currently under development.

In addition to the oral and poster presentations at the IACFSME conference, CDC's program is also co-sponsoring a workshop with the American Academy of Physical Medicine and Rehabilitation on addressing ME/CFS like symptoms in Long COVID patients.

We are also planning another CDC COCA Call in June on how primary care providers can assist Long COVID patients in returning to work. Speakers will be from CDC's National Institute for Occupational Safety and Health and the American College of Occupational and Environmental Medicine.

One of our other projects, COVID-RELIEF, which stands for Research on COVID Long-Term Illness, Effects, and Risk Factors, in partnership with the University of Washington tracks electronic health records of patients who test positive and negative for the virus that causes COVID-19, and documents symptoms and medical conditions for about two years after that

infection. A subgroup of patients who previously tested positive for COVID report on their ongoing health symptoms and provide blood and saliva specimens to help us assess whether there are genetic and other risk factors that may lead to delayed recovery from COVID. Multiple analyses using these data are ongoing. A manuscript on incidence and predictors of fatiguing illness following COVID-19 should be submitted for publication soon. We're excited to have reached the stage of being able to disseminate the findings of the Long COVID projects that were initiated during the earlier phases of the pandemic.

Before we turn it over to our guest speaker, I'd like to remind you that if you have suggestions for speakers or ideas for other topics for future S-E-C calls please e-mail us at M-E-C-F-S S-E-C@CDC.gov. You can use this address to be added to our email notifications about upcoming calls. And finally, a reminder that the transcript of this program update, along with a full transcript of the entire S-E-C call will be posted on our ME/CFS website.

Now, I would like to introduce our guest speaker, Dr. Jacek Skarbinski, Dr. Skarbinski is a physician research scientist at the Kaiser Permanente Division of Research and a practicing infectious diseases and HIV medicine specialist at Kaiser Permanente's Oakland Medical Center. He is part of The Permanente Medical Group Physician Researcher Program and serves as co-chair of the Kaiser Permanente Northern California COVID-19 Clinical Research Coordinating Team. Dr. Skarbinski has been working on the ME/CFS consultative service at Kaiser Permanente since 2020 and has been engaged in ME/CFS epidemiologic research since 2019. Dr. Skarbinski earned his M.D. at Stanford University School of Medicine after completing his B.A. at Cornell University. He completed his internal medicine residency at the University of California-San Francisco in the San Francisco General internal medicine primary care track. He served as an Epidemic Intelligence Service officer at the CDC and completed an infectious diseases fellowship at Emory University School of Medicine. He is the Kaiser lead investigator on the CDC-sponsored Emerging Infections Program Project Surveillance to Optimize Protocols for Early Identification and Subgrouping of ME/CFS, which we've shortened to "STOP ME/CFS" and the COVID Standardized Evaluation of Long-term Effects (also called COVID-SELECT). His presentation today is entitled, "Myalgic Encephalomyelitis/Chronic Fatigue Syndrome-like Illness Following COVID-19 in a Large Integrated Health System: Findings from the STOP ME/CFS Study." Welcome, Dr. Skarbinski.

Dr. Jacek Skarbinski: Thank you. Thank you. It's a pleasure to be here.

Great. I think you can see my slides right now.

Thank you, so much. It's a pleasure to be here. So, my name is Jacek Skarbinski. I work for Kaiser Permanente, Northern California, and just to tell you a little bit about our health system. It is a large integrated health system. We serve over 4.6 million people across Northern and Central California, and we have existing hospitals, existing hospitals, over 22 hospitals and 250 medical clinics that serve all of the patients in our catchment areas, and we provide all

preventive and curative clinical services to this population. And today I'm going to be speaking about sort of two of my big research areas and things that I'm, I'm very passionate about, myalgic encephalomyelitis/chronic fatigue syndrome or ME/CFS and COVID-19 and that intersection.

So, we can agree that ME/CFS causes substantial morbidity. And however, when we look at our health system and many health systems we've always recognized, that we both under diagnose it, so patients who have ME/CFS are not recognized by the health system and don't receive care in the in the clinics, or over diagnosed, patients have diagnosis in the chart of ME/CFS, who don't necessarily meet the diagnostic criteria. And in around 2019, through my colleagues, Dr. Champsy, who is very active in our clinical program, we were approached by the CDC, and we started working with the CDC to think about how to tackle this question. And we started off with designing a study to try to figure out how much ME/CFS is in our health system, and we realized that we needed to do something that includes patient self-report. We realized that it couldn't be based on medical records. We are a large medical system. We use a lot, and we do a lot of our electronic medical record studies. For this type of study, we really needed to go out to be able to somehow capture patient experiences.

The question was there's 4.6 million people in our system of about 2.7 million adults. How are we going to talk to all of them? We can't. That's a, that's a gigantic study, and ME/CFS in standard prevalence studies done by CDC, and others is about half a percent to maybe up to 2% in the population, which means we would have to reach out to a large number of people in order to be able to recruit persons who had ME/CFS. So, we set about thinking about how to use the medical record and how to create a risk, or and use the data we have in the medical record to try to identify persons who might have ME/CFS, and that's what we spend 2019, that's what we spent on in 2019. And then, unfortunately, something happened. COVID happened. SARS-CoV-2 emerged, right?

March of 2020 SARS-CoV-2 emerges pretty much as soon as we, as soon as, very soon after the first cases of SARS-CoV-2 we recognize that people are having long-term symptoms. But by the summer of 2020, and definitely by the end of 2020, we are hearing Post-COVID Conditions. For those of us who have worked on ME/CFS, you recognize that, hey, viral triggers have been associated, or have been a trigger, for ME/CFS.

COVID could be one of these triggers, and so we went back to the drawing table and redesigned how we were going to tackle this. And we basically created this study that tries to get at both questions. And we basically decided that from our big HER [health electronic record] system for about 2.7 million people, we're going to try to find everybody who has a diagnosis to see if we can confirm their diagnosis. Everybody who's got a post-COVID conditions diagnosis. We're going to use our high-risk score that we developed earlier to try to find persons who might be, or have some records, some things in our health systems that suggest that they might have, ah,

chronic fatigue. Things like, for example, multiple fatigue diagnoses reported in medical record, multiple visits for fatigue. And then we that took everybody else and looked at them. Those who had COVID and found a group of people who did not have COVID.

In 2022, we reached out to almost 100,000 persons at Kaiser, Northern California, all adults, and enrolled 9,800 people. They um all did. We had electronic medical record information, and we did a very detailed electronic survey with self-reported symptoms, symptoms that allow us to classify whether or not they meet the criteria of ME/CFS, the IOM criteria, also looking at, other symptoms, they might have functional status, and then scale mental health assessments and others. So basically, a wide battery of tests that let us both make a diagnosis, or make us identify people who might have had ME/CFS, or what we call ME/CFS-like illness, because we're not making a diagnosis and assess their, their other characteristics. And based on this questionnaire and the data that we have in hand, we basically looking at duration, so more than six-month frequency, moderate or severe frequency, severity, moderate a severe severity, just like the IOM criteria,we are able to identify people who have ME/CFS-like illness, and then we group them into two groups. One group that basically said, look, we have everybody's COVID history. They said, these symptoms all started after COVID after my COVID episode, and we identified a group of patients who report ME/CFS-like illness symptoms after a COVID-19 episode. We found another group of patients who had ME/CFS-like illness, met all the criteria, but was completely unrelated to COVID. Ah, they may or may not have COVID, but the symptoms were predated COVID or unrelated to COVID. And the last is a large group of patients who, who did not have any ME/CFS-like illness.

And this is what we found. So about 50% of people in our system, so, 2.6 million people just to give you big numbers, 2.6 million people, half of them had COVID. So, 50% of our population has had COVID basically, is that have at least one COVID episode., The other half did not have COVID. And if you look at this, about 2% meet the criteria for having ME/CFS-like illness. Okay. So, severity, frequency, duration of symptoms of all the categories. When you break that down about six thousand, so it's about one in two hundred people who've had COVID, report symptoms after their COVID episode that are consistent with meeting all the criteria, duration, frequency, and severity for ME/CFS-like illness. And the rest, about 4,400 people, have ME/CFS like illness in our system but is unrelated to COVID.

And so, for the rest of the study we're going to compare these three groups. We're going to think about how they're similar and how they're different. So almost every single slide is going to be set up in the same way. We're going to be comparing these things. And so, column one, here, is chronic fatigue syndrome after COVID-19. Column two is without COVID-19, and column three is no ME/CFS-like illness.

So, first thing I want to point out is that obviously in the first two columns everyone has 100% on the, on the, for fatigue post-exertional malaise, and unrefreshing sleep, because they have

to for the diagnostic criteria. But you can see that orthostatic intolerance, right here, is much less common in the group that has an ME/CFS-like illness after COVID-19.

And then the last thing is, I want to look at duration of symptoms in our group, that is, that has ME/CFS-like illness after COVID-19. Duration of symptoms is about two years, which makes sense because the pandemic is, were about three years into it right now, whereas the other group has a very long duration of symptoms approximately nine years. So, they've been, they've had, they've had fatigue, symptoms, and other symptoms for approximately nine years. Also, I want to point out that in the people who do not meet criteria at all, about 19% report, severe, severe, frequent fatigue. And then about 26% unrefreshing sleep. So, these are fairly common symptoms in the general population.

So next, I want to kind of go through the demographic characteristics, and the first thing I want to point out is that this group that has ME/CFS-like illness after COVID-19 is younger. Average age is around 36 years compared to 45, or 50 for the other two groups, and they are more likely to be Latinx or Hispanic. About 45% of them.

There is a, ah, female sex predominant for both groups, and then, ah, there is some relationship with obesity. We have a higher percentage of people in both groups with ME/CFS-like illness who have a BMI or body mass index greater than thirty.

And then, lastly, a little bit about their sort of COVID history. So, this group of people who have ME/CFS-like illness after COVID-19 are slightly less likely to be vaccinated. Only about 75% compared to 90% plus. And then most of the infections, when we contract down exactly when their infection occurred, we have pretty good tracking of what variant is circulating, what time period. So we use calendar time to carefully describe which variant you are most likely to be infected with. About 74%s had their episode of COVID-19 that precipitated this relationship with developing ME/CFS-like illness during the pre-Delta period—so before Delta, before Omicron.

So next we assessed symptoms severity and look at differences and symptoms. And again, we're always comparing the three groups. And just to kind of orient on your slide, so, this is percentage of people with symptoms is on the Y-axis. The symptom categories there are on the X-axis. The symptoms are organized in the sort of order of frequency that they're seeing in people who do not have ME/CFS-like illness. So, think about it. Reference, population, comparison group. And you can see, for example, in the first column here, first of our set of bars, here muscle aches and pains are common, maybe in 18% of the general population people without illness, but that's much more common in both, in people with ME/CFS-like illness after COVID-19, and ME/CFS-like illness without COVID-19. And you can see that both groups of patients are more likely to experience almost all of these symptoms. And this is by the way, we've actually filtered this out so, these are symptoms that meet certain severity. So, they're moderate to severe on severe, on the severity scale, and moderate to severe frequency. So, this

is a pretty substantial symptom burden, and you can see that for every group here that both patients with ME/CFS-like illness after COVID-19, which is in the light green, are higher, more likely to have these symptoms than people who do not have any ME/CFS-like illness. And same thing for people with ME/CFS-like illness without COVID-19, also, substantially higher. And when you compare the two groups, those who have it after COVID-19 or chronic fatigue syndrome after COVID-19 have, seem to have, a slightly lower symptom prevalence than people with an ME/CFS-like illness who did not have COVID-19.

Next, we did the sort of the same comparison, and the setup is here is exactly the same. The charts are set up in the same way. But here we're looking at physical, emotional, and social functioning. Same set of setup. This is a t score. This is a score fifty is about average, so if you survey the general adult population, most people score around fifty on this. This is normalized. So, fifty is the average um, and you can see that the ah, the ah, categories are again organized with decreasing scores for the group that has no ME/CFS-like illness. And you can see the two bars that both patients, patients with chronic fatigue syndrome, whether after COVID-19 or without COVID-19, have much lower score—significant and substantially lower scores for both pain, physical function, energy, fatigue, emotional well-being, general health and social functioning with, for. In most cases both groups of patients, with COVID-19 and without COVID-19, having similar levels of impairment except for pain, where one group appears to the those with ME/CFS-illness after COVID-19 appear to have less pain or higher, uh, less pain than those with ME/CFS-like illness without COVID-19.

Next, we looked at the sort of anxiety and depression, and again, this, this the chart here is set up in the same way. Those without chronic fatigue syndrome are in the dark blue here on the, on the right, and you can see that around 20% of them meet criteria, diagnostic criteria through either PHQ-8 or a GAD2, for depression or anxiety or anxiety respectively; whereas both groups with chronic fatigue syndrome whether after COVID-19 or without COVID-19 have substantially higher scores and almost 70-80% of them meet criteria for either depression, moderate to severe depression, or moderate to severe anxiety.

And lastly, I want to talk a little bit about occupational status, and this is the ability to engage in the workplace. The charts are set up in exactly the same way. Those without chronic fatigue, or chronic fatigue-like illness, are in the dark blue on the on the right. And as you can see, I think the most important thing is that when you look, when we look at the group that's unable to work through the disability, patients with ME/CFS-like illness that's not associated with COVID-19, remember duration of symptoms, average duration of symptoms is nine years, about 24% of them have had to go on disability because they're no longer able to work compared to the other groups, which around 2%.So much lower engagement in the workforce.

Notice that those with ME/CFS -like illness after COVID-19. So, they've got all the symptoms. We've seen the symptomatology in the first slide we've seen the ah, the ah impairments and

physical, social, emotional function scores on this. On the next set of slides, you'll notice that that group is younger and actually still more likely to be employed.

All right so, I want to kind of take it back, and I want to take us a little bit through a little thought exercise and summarize here. So, the main takeaway point from this, what we're looking at is that the burden of ME/CFS-like illness after COVID-19 might be very large, and I did a little math here for us to show us what this looks like in our kind of study. We got about 2.5 million people, but I showed you 50% of them had COVID-19, and I say that one in two hundred develop ME/CFS-like illness after COVID-19. I did the math for us here, and we have about 6,700 people, which doesn't seem like that much, but I want us to multiply it out for the United States and think about what the burden of this might be in the United States, and the scale of the problem that we might be seeing. We have 258 million adults in the United States. Our statistics here, and approximately is that probably, about half the US has already had COVID-19. If we apply this one in two hundred, we'll develop a ME/CFS illness after COVID-19, we're going to get about 670,000 people. I've added a confidence interval in there because our estimates of population-based estimates. I could spend hours talking about how we produce them, but they are designed to produce population-based estimates, so real world estimates of what the burden might be. We're looking at a 670,000 and the estimates, maybe between 177,000 to 1.1 million. This is a really large number of people. Remember that the US has experienced about 1.1 million deaths overall from this. So, this is a large group of people that might have ME/CFS-like illness after COVID-19. And then the last thing I want to leave us with is, if we think about, what are we seeing, we've shown, and we just studies really showing a very high symptom burden. This is six months out, so this is already after the initial episode, more than six months after there, so real impairment and physical, emotional, and social functioning, and real increases in depression and anxiety. I would like to thank the CDC for supporting this work, as well as the NCI and the NIH, and my local institution.

And I'd love to take questions. I think I'm going to stop sharing. Yes.

Christine Pearson: Thanks for that presentation, Dr. Skarbinski. We'll now move on to the Q&A portion of our call. There are three ways to ask a question. If you are joining on zoom, you can raise your hand by clicking the "raise hand" button under the webinar controls at the bottom of the screen. Or you can type your question in the chat box, which is being monitored by the CDC team manager on this call. If you're joining by phone only, you can enter "star 9" on your phone to join the question queue, and when we announce that it's your turn, press "star 6" to unmute yourself.

While everyone gets a change to submit their questions, I'll go ahead and kick us off with a question that came through during the presentation. So, Dr. Skarbinski, has this project influenced how Kaiser approaches ME/CFS?

Dr. Jacek Skarbinski: Yeah, it's been, it's an interesting journey. You know, our, our, how we're thinking about our clinical care actually mirrors how we're thinking about our study, because we started out as a ME/CFS consultative service and trying to provide services and trying to educate all of our providers about how to identify patients, and then how to do standardized assessments and provide care across our very large geographic area. Just to give you a sense, we're a very large system, we got a large geographic area. So, it's like eight-hour drive, whichever direction you go in order to, to see, so providers and providing services. I told you 22 medical centers, 250 medical facilities. That's a huge breadth. So, we're working hard. We're working hard to organize that. And then COVID came. And you know, when people first describe Post-COVID Conditions and three years in, we're still sort of halfway there and deciphering this. It's a very complicated problem, because people are describing everything. Some things that matched chronic fatigue syndrome, but many things that were unrelated to chronic fatigue syndrome, and people have described, and organ diseases so thromboembolic disease, myocarditis, pulmonary disease, acute lung injury, things that are pretty much have a home somewhere within the rest of medicine. There's some sub-specialty that takes care of it, cardiologists, pulmonologists, hematologists, and then other symptoms that are clearly chronic symptoms, new findings, but are different than chronic fatigue syndrome. They don't meet the criteria, and I think we've been, we actually had, started two programs. So, we had a post-COVID conditions program and a chronic fatigue central program. And now, based on this, we're thinking about how they overlap and how they merge, and I wouldn't be surprised. And I don't know we'll know by the time we finish this study, because we've got a few more pieces to it. Where really the, the bulk of our care is going to be in this population treating chronic fatigue syndrome.

Christine Pearson: Great. Thanks so much. So, the next question is I think a little bit of a clarification question and I think it's important to may ask this now before the rest of your answers, so the question is: what is meant by ME/CFS-like illness versus saying ME/CFS illness?

Dr. Jacek Skarbinski: That's a great question. And so, we use this, this phrase: ME/CFS-like illness because we are not interacting with every single, all 9,000 plus, 9,800 plus participants in our study. We are using their survey responses, what they say on a, on a, survey. We're using the same criteria. But we are not doing a clinical diagnostic evaluation, and that's actually really important, because there may be some people who report all of the symptoms who may not have chronic fatigue syndrome per se, but another condition. And we we're not able to tease that out, because we don't have a clinical component, and I do feel that chronic fatigue syndrome, ME/CFS, to make a diagnosis needs to have a clinician preferably trained with experience with ME/CFS making that diagnosis, that I don't feel comfortable making that on a survey. But they clearly meet all the criteria, and as we've shown you, they have many of the sequela that we would expect.

Christine Pearson: Um, Thank you. Uh. So. The next question is, uh, what do you make of the differences you found between people with any ME/CFS-like illness after COVID versus people with ME/CFS-like illness without COVID? Might the length of time with ME/CFS account for some of that difference, or the differences?

Dr. Jacek Skarbinski: Yeah, that's a great question. I think that's a large part of it, and a lot of what we, when we started out thinking actually is, can we find people who are early in their disease course? This is pre-COVID. This is one of the big questions we had. I think that is the, the duration of symptoms is a large component of that, two years versus nine years. I will give you a very specific and clear answer in about six to nine months, because we are doing a repeat survey of everybody. We are in the process of redoing, of doing a reassessment of everybody in terms of, ah, symptoms, symptoms, functional scales, et cetera, and I think it's going to be very important to understand really well how well we're doing in terms of the stability of these symptoms over time. So, I think we're going to, we're going to have a better answer to this question. But I think duration of symptoms is the big, is the big, difference.

Christine Pearson: Okay. Great, thank you. So how is ME/CFS diagnosis documented in the Kaiser medical record, and what are your expectations about being able to track diagnosis of ME/CFS going forward?

Dr. Jacek Skarbinski: That's a great question. So, we use standard ICD-9 and [ICD] 10 diagnosis codes. We actually have an overlay on top of them in terms of we have, we have a much more, much richer diagnosis code list that will map onto a single diagnosis code labels, I guess I would call them, that would match onto, the match onto the diagnosis code itself, because ICD-9 and ICD-10 , which are required to use in American medicine, are rather limited in some ways. So, we have our own labels that we use. We're working hard to try to get some real sense specificity to our diagnosis codes, and who we diagnose.

Christine Pearson: Thank you. So, the next question is, it looks like from your graphs that, that the group ME/CFS with no COVID may be sicker than even the after COVID group. Is this a reasonable observation? And if so, do you have any hypothesis why this may be the case? Does it have to do with the duration of the illness?

Dr. Jacek Skarbinski: Yeah, as I mentioned before, I do think that the duration of illness is the key, is the key element to why those two groups look different. There's also some differences in age. One is younger than the other, but I think duration of symptoms is probably going to be the big driver.

Christine Pearson: Okay, great. Thanks so much. So might depression or anxiety infection induced ME/CFS be caused by the interferon response to infection?

Dr. Jacek Skarbinski: Ah, this is a great question. I don't know the answer. There, traditionally, ME/CFS is not considered, is not considered to have, you can, you're allowed to have co-morbid

depression or co-morbid anxiety so you're about to, it's possible to have both, but they are unrelated. Ah, per se. Now, I don't know in this study what why we were seeing. We're certainly seeing a lot of anxiety and depression symptoms, and we're definitely going to explore that further.

Christine Pearson: All right. Great. Thank you. So next from our folks who have their hand raised. I have one. It doesn't have a name, but it's a 6-4-6 number that ends with 1-2-5. Give you a second to unmute. Okay, we will.

Erik Johnson: Hi there, Erik Johnson here.

Christine Pearson: Yeah, okay.

Erik Johnson: So, I'd like to say that I'm an incline village survivor, the original prototype for chronic fatigue syndrome.

*1646****125:* Hello? Hello?

Erik Johnson: Hello?

*1646****125:* Hello, sorry I was asked to unmute.

Christine Pearson: Yes. Please go ahead. Ma'am? Are you still here?

Christine Pearson: I'm sorry about this. I don't have names. Okay. Why, don't we um sorry about this everybody. Let me for me. I got to ask you to unmute signal.

*1646****125:* Yes, hi. I just unmuted. Can anyone hear me?

Christine Pearson: Yes, yes. We can't. I'm sorry. Um, okay. Um. Let me, let me go to, uh, to a different room real fast, and then we'll see if we can get that figured out. I'm sorry everybody for the, for the problem. Um. So uh, this question, I think, is, I think, is meant for CDC. So, it says, um, studying Long- COVID alone does not help people with ME. Will you be including ME patients in your studies that have Long COVID patients.

*Dr. Jennifer Cope: Y*eah, this is Jennifer Cope. I can speak to that. So, one of the, in my in the update one of the studies I mentioned, um, the COVID-UPP study is one that comes to mind. That is a study that's being done specifically doing some of the same, uh, tests in the Long COVID patients that have been done in the MCAM study. And so, the intent there is to be able to compare similarities and differences among Long-COVID and ME/CFS patients.

Christine Pearson: So, the next question that we have, I think, is for you, Dr. Skarbinski. So, it says people with severe ME/CFS are housebound and/or bedbound, was this patient population included in your evaluation? And if so, how?

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Dr. Jacek Skarbinski: Yeah, that's a, that's, that's a great question, and it's something we're very sensitive to. So we are, we this is all electronic so, no one had to go anywhere. So, this was all, this was all we did electronic and phone recruitment for this study. And again, we wanted to get out of our health system. We wanted to hear what people are about. Our patients are feeling without necessarily needing to come in. For patients who expressed the need that they were not able to complete a computerized survey on their own, we provided assistance to that. So, our research assistance provided assistance with that to be able to help them complete a survey. If they said they wanted to do it, we would provide the assistance for that.

Christine Pearson: Thank you so much. So. Um, Dr. Skarbinski have you also looked at, or will you look at, the group of Long COVID patients who do not meet your criteria for ME/CFS-like illness. If so, how do those compare to your two ME/CFS groups?

Dr. Jacek Skarbinski: Excellent question. And we've just started looking at that data to try to, to all of that information, to try to tease that out. I don't know yet. I will know in a few weeks as we, as we sort of digest it all and try to try to figure it out. Remember half our members, so, half the people have had at least one episode of COVID in our system, which is similar to probably anywhere else in the United States. So, it's a really large group. So, we're really trying to tease that out. But that's a very important question.

Christine Pearson: Thank you. So, I think we're going to try this hand thing again. I apologize in advance, but it doesn't work. So, whoever was the 1-2-5 at the end, if you like to try again.

*1646****125:* Yes, hi! Can you hear me? This is Eileen Holderman.

Christine Pearson: Yes, we can.

*1646****125:* thank you.

Eileen Holderman: My name is Eileen Holderman. I'm an advocate for ME and I'm a former ME/CFS advisory committee member. Thank you for this call and thank you for the presentation. My question is for Dr. Skarbinski. You mentioned the number of times the IOM SEID criteria, and I don't know if you're aware, but advocates have been protesting that since 2012, 2015 because we feel like the criteria is a simple checklist of four things, and doesn't even begin to describe the magnitude of this infectious disease, this neuro-immune disease. And so, I'm wondering why you used a non-expert criteria when there's already one available, called the ME ICC, the International Classification International Canadian Criteria. Thank you.

Dr. Jacek Skarbinski: It's a great question, and, and you know, and I'd love to, I'd love to learn more. Um, we use the IOM criteria to have a starting point, and I recognize all the, the concerns about the diagnostic criteria, about sensitivity, specificity, and that it doesn't fully capture the full, the full spectrum of symptoms with ME/CFS. That's the short answer: because we needed a starting point. It is the accepted criteria in the United States. Um, we're doing a lot of work to

really think about actually all of the associated symptoms, and both as a clinician and as a researcher, I would say it's the, I call it the penumbra to sort of like associated symptoms that are not in that IOM criteria that are, are a very large cause of morbidity. And we're really interested in trying to figure tease them out and see which ones we are, how to put them all together, how to think about them, and then, most importantly, how to treat them to, ah, improve patient's quality of life. So very point, very, very well taken, thank you.

Christine Pearson: So, my question is, is there any medical reason for diagnosing individuals with Long COVID instead of ME/CFS? Other than a severity of symptoms which may be due to shorter duration of condition. Is there any medical distinction whatsoever?

Dr. Jacek Skarbinski: Yeah, I, it's a great question. I think this is where we this is in it, and relates to the second question, you know, is clinicians, providers, researchers, we need sort of some, some guidance and criteria. I think it partially depends on what people are coming in with, and what they report whether they're reporting the symptoms and they are saying, ah, they're related to COVID or unrelated to COVID how they're going to get, how we're going to, how someone might diagnose them with post-COVID conditions versus ME/CFS. I think this is where, I know the NIH is putting out a call for this, and people are really looking at kind of creating a, a, set of consensus criteria, and again goes back to the other comment. Having well done, diagnostic criteria is going to be really helpful, and thinking about the full spectrum, just because you mean X number of symptoms doesn't ever describe you as a whole person in any for any disease process. So, I want to just be clear that that's, that's you know medicine uses small labels, but that doesn't just mean that. But it, it never describes the whole person, and we vary. We understand that in this condition and all other conditions.

Christine Pearson: Thank you. So, the next question is, was there anything in these data that surprised you? You mentioned comparing patients with different duration of illness. What else is next?

Dr. Jacek Skarbinski: Ah, so our next steps are big things that we're really interested in. Number one is repeat survey, and we're planning on, we're in the process of re-interviewing or reassessing everybody this year since we, one year later and hopefully next year and the year after, that's first. So that's really understanding stability of symptoms and duration of symptoms and changes in severity. That's number one. Number two is really teasing, about teasing out the, for those who do not have chronic fatigue syndrome after COVID-19, what are the true symptoms burden, and what are the differences and symptoms that people get after COVID and thinking about COVID-19 as the incident event that then leads to certain other things, and it's really important. Again, remember, 50% of the country had it. This is huge numbers of people have a COVID-19 and will have COVID-19. So that's number two. And the third is really trying to understand the associated symptoms and trying to tease apart what other conditions are associated, and we really have a lot more work that we're doing around

things like pain, things like IBS, things like fibromyalgia, other associated conditions which cause again, as I mentioned, substantial, substantial morbidity, and if we had better solutions for could really improve patients' lives. Those are the kind of three big buckets we're working on next.

Christine Pearson: Thank you. Um. So, the next question is, what a portion of people that you identify with symptoms had an ICD code in their record that pointed to ME/CFS? Do you identify a lot of people who are not actually diagnosed with ME/CFS?

Dr. Jacek Skarbinski: Yeah. And this gets at the this gets at this question of diagnosis, under and overdiagnosis. So, a very small number of patients, and I'm going to say 2%, 3% of patients had either a post-COVID conditions diagnosis. And this is what used to be PASC, post-acute sequelae of COVID. This was the first set of codes that came out, or an ME/CFS diagnosis in the chart. So very small. So, this is kind of why we're kind of thinking a lot about this over and under diagnosis question. These patients are out there. We are not meeting their needs. We need to think about how we are, how we're finding them, how their needs are getting addressed in the health system, and how we, as a health system track it, and I know diagnosis codes are not the most interesting, I think, out there, but they're actually extremely important for, for any clinical enterprise, for any health system is to have a sense of a clear sense of who's getting diagnosed, and who's, who's not getting diagnosed.

Christine Pearson: So, the next question is about variants. It says, um could the results that show the significant number from pre- Delta variant be the result of lack of vaccination? The six-month requirement to obtain a ME/CFS diagnosis, and or the delay many folks are having an accessing care post infection.

Dr. Jacek Skarbinski: I think the variant and vaccination question is going to be extremely important. Um, we have sort of early signals that suggest that vaccination, and even in one of our more in-depth analyses that I haven't presented here, that vaccination might be protective, for that, having had an episode of COVID after vaccination might be protective. So, vaccination is protective from developing post-COVID conditions, and in this case ME/CFS. So that's one thing. So, I think vaccination is really important, and as we scale a vaccination in this country that might make a big difference. That's number one. And I do think the variants are really important. We do a lot of other work on SARS-CoV-2, the virus that causes COVID-19, and we certainly see very different manifestations of severe disease after everything that came before Delta, Delta, and Omicron, and I do think variants might actually play a very important role. Good news might be that Omicron might be, which is more transmissible. And what think about estimates. Around 40% of Americans have been infected with Omicron that, ah, Omicron might be less likely to cause to be the incident trigger for potential ME/CFS or other post-COVID conditions. We can't say that definitively. But I think that's where there's some evidence from us, and from others to suggest that.

Christine Pearson: Excellent. Thank you. Do you have any indication whether or not there's a greater risk of Long COVID or ME/CFS with repeated COVID infections?

Dr. Jacek Skarbinski: It's a great question. It's, stay tuned for our next analysis. That's the one we're doing is trying to really tease apart, who develops symptoms after a COVID episode? And what are those risk factors in terms of really thinking about vaccination, repeat episodes. Quite frankly, it could go both ways. Because you do develop some naturally induced immunity from, ah, from infection. So, I don't know the answer to that. So, we're going to, we're going to have to see.

Christine Pearson: Okay, I think we're going to try to do another hand, hopefully, this will work. I'm going to try to take a call from Bridget. You try to unmute, please, or maybe it says maybe it's Liz, I'm sorry I can't, having technical difficulties here.

Liz: Hi, if it's Liz I'm here.

Christine Pearson: Hi, Liz. We can hear you.

Liz: Terrific. Yeah. Yeah so, my comment is for Dr. Cope, and let me just say, thank you, Dr. Skarbinski, for doing the work. But Dr. Cope, I want you to know that I live here in Atlanta, and we had multiple people go to the CDC to see the blue lights. You were going to light up the Atlanta campus, and multiple people go to the campus to see the blue lights. We've failed to see any lights. This is emblematic of what we've come to expect from the CDC. You'll diminish your credibility when you say you're going to light up the campus that gives us awareness, and nobody saw the lights y'all. So, for you to reframe it as highlighting your efforts to recognize this on May 12th, it just doesn't hold water.

And I say this with respect. You are burning bridges with your most, with your best allies, with your best friends. I need you to succeed because my life depends on it. You had a gentleman call in earlier who was unable to speak. He said he was from the Incline Village outbreak. He's been here since the 1980s. There's got to be more urgency from your end.

Christine Pearson: Thank you for your comment, I appreciate it. So, the next question is, there's an ME/CFS clinic within Kaiser and developing Long COVID clinic. What clinic do you feel is best equipped to serve post-COVID ME/CFS patients?

Dr. Jacek Skarbinski: Ah, that's we're actually actively thinking about what the best, what the best way to tackle this is. And actually, I think, because a lot of what we're thinking about post-COVID is changing right now. And that that field is rapidly developing. So, I think we're thinking about it. I don't have a I don't have a off the top answer, best solution.

Christine Pearson: Um, let's, let's go on. I apologize in advance. We have a ton of questions. I don't think we're going to be able to get to everybody. So, the next question is it, uh is, what is the treatment protocol for those with ME/CFS? And I'm, I'm not clear if this is um for CDC or if

this is for you, Dr. Skarbinski related to your study. Do you, would you like to um take it first um answer to that?

Dr. Jacek Skarbinski: Ah, I guess I, that's a little bit of a vague question, so I'm not sure. I'd have to need a I need a little bit more detail about which aspects we're talking about.

Christine Pearson: All right. Okay. Sorry about that. Um. So, it seems like existing disease burden is much worse due to ME/CFS before COVID. So, if 50,000 affected total, I think Kaiser needs at least one MD per thousand patients. Can Kaiser train 50 ME/CFS doctors with expert training, such as the Bateman Horn Center.

Dr. Jacek Skarbinski: Ah, great question. So um, we're scaling up. So, if you're asking about the clinical program. We're scaling it up and thinking about how to best organize it. We are definitely going to be different and ah than a clinic, like the Bateman Horn Center. Ah, partially we, we serve a distributed population across a large geographic area. So it's thinking about how to make sure that we have, ah, providers, knowledgeable providers, across the spectrum, and that are geographically located. We use a consultative model primarily in partnership with a lot of the specialists we have already locally based, and that's primarily not to have patients to travel to a single location, or even two or three locations. Ah, but that's going to be our model and model is always going to be a partnership model with providers, not just any ME/CFS specialists, ME/CFS specialists, but specialists across the board. And because many of the treatments, and someone asked about treatments, it's kind of hard to describe all of them, are going to be dependent. Some may involve neurologists, cardiologists, physical therapy, occupational therapy, et cetera. So, we're going to a mental health, psychiatry, behavioral health. So, we're going to use it. A network of providers across the board for what the patients need.

Christine Pearson: All right. Uh, the next question is where do patients fit into these groups who did not have a positive test for COVID but had a COVID-like illness and developed ME/CFS symptoms after 2020?

Dr. Jacek Skarbinski: So, we use data to figure out who's had COVID. We use both data from testing, so testing, testing data, tests that were conducted here within Kaiser as well as patient self-report. So, we actually take a detailed COVID history. So, we use both sources of information and cross-tabulate them to assess who has had COVID.

Christine Pearson: All right. Excellent. So then uh, the next question, I think, is the last question we're going to be able to take today. And I think this may be for CDC here. Um, but feel free to jump in if you like Dr. Skarbinski. Where do you recommend that we go for help? What organizations or doctors can provide support for ME/CFS like symptoms post-COVID?

*Dr. Elizabeth Unger: S*o, that is one of our most important issues. And that's why we've been doing what we can to increase educational opportunity. Um CDC does not have a list of

physicians or clinics, or for people that we can recommend for people. Um, but there are other organizations that do provide these lists. Um, and there aren't enough of them. We understand that.

Christine Pearson: All right. So, thank you, everyone for taking the time to join us this afternoon. A reminder that we'll be posting the slides on our website ASAP, and we'll have a video recording and transcript posted as soon as they are available.

We hope you leave with a better sense of information on ME/CFS, and on behalf of the entire ME/CFS program. We wish you the best as we head into the summer months. Thanks so much.