Kate Fowlie: Good afternoon, everyone. Welcome to today's ME/CFS stakeholder engagement and communications call, which we call SEC or “SEC.” My name is Kate Fowlie and I’m a health communicator assisting CDC Division of High Consequence Pathogens and Pathology. This is the division where the ME/CFS program is located within CDC’s organizational structure.

As you know, we host these SEC 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. Elizabeth Unger. She is the Chief of CDC’s Chronic Viral Diseases Branch. Then we'll turn it over to our guest speaker from the University of Pennsylvania's Perelman School of Medicine, Dr. Stephen Gluckman.

After Dr. Gluckman’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. We're also recording this call, so please disconnect now if you have concerns about that. We will post the 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, Kate for that introduction. I'd like to welcome everyone to CDC’s 19th SEC Call. As in the past SEC calls, I’ll start by providing some updates on our program and then we'll hear from our guest speaker Dr. Stephen Gluckman. I want to really thank Dr. Gluckman for taking the time out of his busy schedule to be here with us today and we're glad that everyone can join us for this call. Now for the latest updates. We recently posted the summary report, meeting agenda, participant call list and slide presentations from the third Roundtable meeting, titled “Working Better Together” on our ME/CFS website under the meetings tab.

We continue to focus on better understanding the overlap between ME/CFS and Post COVID Conditions, often referred to as Long COVID. As we've mentioned before the similarities between the two illnesses provides us with a unique opportunity to study and hopefully gain a
better understanding of both conditions. Some of the Long COVID studies that we are participating in were introduced during the December SEC call, but I wanted to provide more updates.

COVID-UPP, which stands COVID, Understanding the Post Viral Phase, is underway. This study is led by Dr. Nancy Klimas at the Institute for Neuro-Immune Medicine at Nova Southeastern University. Her team, in collaboration with several large health centers in southern Florida, continues to enroll patients who have fatigue and other symptoms three to six months after their initial COVID diagnosis as well if patients who had fully recovered from COVID.

The study uses online surveys to gather follow-up information about participants’ health for up to three years, allowing researchers to observe the course of their illness over time. They've piloted the protocol for the in-depth clinical evaluation that includes laboratory testing and cognitive evaluations, with some participants.

A subset of participants who continue to have symptoms following COVID and a comparison group who have fully recovered, will be enrolled in this phenotyping phase to allow a direct comparison of patients with, with ME/CFS.

As part of another study called COVID RELIEF, which stands for Research on COVID-19 Long Term Effects and Risk Factors, our collaborators at the University of Washington are analyzing electronic health records from inpatient and outpatient visits from February 19, 2020, through the end of December 2021 to identify conditions and characteristics associated with severe acute COVID infections or long-term illness after COVID. They will soon begin contacting patients to determine whether they are interested in participating in the second phase of the study.

During the second phase, a subset of participants will complete a questionnaire about their health and provide self-collected blood and saliva specimens for investigation of genetic and other risk factors that may play a role in delayed recovery from COVID. This information may be useful for identifying factors that may cause patients to have different responses to COVID and for ensuring that patients get the right level of medical care.

The first abstract from this study, “Healthcare Utilization and Diagnosis in COVID-19 Patients Followed for Up to One Year,” has been accepted for presentation at the International Conference on Emerging Infectious Diseases in August 2022.

During the last call we briefly mentioned the Long COVID and Fatiguing Illness Recovery Program or LC&FIRP. This is an evaluation project we are working on with the Family Health Centers of San Diego, the ECHO Institute at the University of New Mexico, The University of Washington Post COVID Rehabilitation and Recovery Clinic and the University of Colorado. This project is designed to empower primary care providers to manage patients with Long COVID and similar complex post infectious illnesses such as ME/CFS.
Enrolled healthcare providers will be randomly assigned to either the intervention arm, which includes weekly case-based online mentoring from multi-disciplinary experts, using the ECHO platform, as well as monthly educational webinars held through ECHO or the comparison arm, which includes only the monthly ECHO webinars. The ECHO webinars began in January 2022 and are open to all. The webinars bring together primary care clinicians, medical specialists, patients and caregivers using a multidisciplinary team approach to share emerging knowledge about Post COVID Conditions, ME/CFS and other post infectious chronic illnesses.

Since the webinars began, attendance has grown to more than 500 people per session. Presentations are led by academic medical experts who specialize in conditions experienced by patients with Long COVID such as neurology, pulmonology, cardiology and ME/CFS. Participants can ask questions of the presenters. The webinars also encourage participation by patients with ME/CFS or Long COVID. Information about upcoming webinars can be found online by searching LC&FIRP and ECHO. The URLs will also be available in the materials we post after this call.

As many of you know, one of our programs key activities involves developing continuing medical education, or CME courses, with Medscape. Our new Spotlight CME course, called “A Fresh Look at ME/CFS: Diagnosis and Management of a Multi-symptom Illness” was released in December 2021. We’re excited to report that the course has reached more than 3,600 learners and 1,800 test takers nearly 1,500 of whom have earned the CME certificate.

The course can be accessed through the CDC ME/CFS homepage and links directly to Medscape. We also recently posted a link to the course on the CDC TRAIN learning network to attract more healthcare professionals to this new course. Our website features two other active CME courses, including one by today’s guest speaker, Dr. Stephen Gluckman. His course is titled, “ME/CFS a Case Based Learning Module.” The other course is by Dr. Nancy Klimas, titled “Test Your Strengths and Gaps in Knowledge of ME/CFS.” So far, we’ve educated more than 60,000 learners through Medscape CME courses.

We continue to publish manuscripts based on findings from our MCAM or Multisite Clinical Assessment of ME/CFS study the which ended in 2020. During previous calls we mentioned two of our manuscripts were in journal review. We're happy to share with you that both were recently published. The first paper was published in February 2022 in the Journal of Translational Medicine, titled “Physiologic Assessment of Orthostatic Intolerance in ME/CFS. This paper assesses orthostatic intolerance, using a tool called the NASA lean, a clinical tool shared with the MCAM group by Dr. Benjamin Natelson.

The second paper was published in March 2022 in the PLOS One Journal and is titled, “Cardiopulmonary Metabolic and Perceptual Responses During Exercise in ME/CFS: a Multi-site Clinical Assessment of ME/CFS (MCAM) sub-study. The paper focused on response to exercise in patients with ME/CFS. Dr. Dane Cook, the lead author on this paper, presented data from this study during our SEC call in May of 2021. You can find the call transcript and additional
information on this on our website. Other papers in progress include those on Natural Killer cell function, cognitive testing and a comparison of patient characteristics using standardized measure. We continue to work with the survey experts from American Institute for Research to validate the use of PROMIS measures of sleep and pain in people living with ME/CFS. We expect to have at least three of these manuscripts published next year.

The ME/CFS program continues its partnership with the National Association of School Nurses to collect information about ME/CFS in school children. The first phase of the School-Based Active Surveillance or SBAS came to a close in September. We’re working on a brief paper to share what was learned from the feasibility assessment of this process, using the phase one data from six pilot sites.

During the second phase of this study, we will expand to include more schools and refine the process to enable more schools to contribute childrens’ health data. As part of this partnership, school nurses are educated about the symptoms of ME/CFS and how to identify the illness among students. School nurses from participating schools will collect data on chronic absenteeism and chronic conditions, including ME/CFS and its core symptoms, along with diabetes and asthma during the next three years.

Yesterday, we along with many others, observed International ME/CFS Awareness Day. CDC participated in ME/CFS Awareness Week by increasing social media posts, updating the CDC ME/CFS features webpage and adding a podcast. Visitors will find several updates to our ME/CFS Awareness webpage including recent program updates and information about ME/CFS and Post COVID Conditions. We've been very active on social media and frequent Tweets through the National Center for Emerging and Zoonotic Infectious Diseases Twitter account, and we will continue to post articles and information for the remainder of this month.

For the first time, I went into the audio booth at CDC to record a podcast about ME/CFS. In particular, I wanted to encourage audiences to listen and learn from people living with ME/CFS. You can assess the podcast on our ME/CFS website, or on the CDC podcast page. You can also find it on Twitter by going to @CDC_NCEZID and be sure to share and like the Tweets.

Our Voice of the Patient series continues to grow as more people with ME/CFS come forward with a willingness to share their stories. We posted our eighth story in the series; a married couple shares their first-hand account of life with ME/CFS and the impacts it has had on their relationship. These stories have had hundreds of thousands of views during the past three years.

Lastly, we're excited to announce the rollout of results from our partnership with WebMD. During 2021, our program worked with WebMD to launch an online survey about knowledge, attitudes and beliefs of ME/CFS in the general public. WebMD will highlight the results of this effort on the feature webpage, along with the video interview on its website.
Dr. John Whyte, Chief Medical Officer of WebMD interviewed Dr. Valerie Montgomery Rice, President of Morehouse School of Medicine and Ashanti Daniel, a woman living with ME/CFS. During this interview, we hear perspectives on the survey findings and the video interview will be posted on WebMD/ Medscape website for a year. We hope it draws attention to ME/CFS and how the results could help research and clinical practice.

As part of this collaboration with WebMD, I participated in an interview with Dr. Hector Bonilla from Stanford University, who was the speaker for our December SEC call. We both commented on the survey results and the need to reach out to different target populations that are not yet benefiting from early diagnosis or education about ME/CFS.

And now I would like to introduce our guest speaker, Dr. Stephen Gluckman. Dr. Gluckman is a professor of medicine at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia and Medical Director at Penn Global Medicine. He received his medical degree from Columbia University, completed his residency at the hospital of the University of Pennsylvania, and has been in practice for more than 20 years in both infectious diseases and internal medicine.

He's the author of the Up-to-Date article, “Clinical Features and Diagnosis of Myalgic Encephalomyelitis, Chronic Fatigue Syndrome.”

Welcome Dr. Gluckman.

Dr. Stephen Gluckman: Oh, thank you, I think I should share my screen right. So, you have to stop sharing if I'm going to share. Okay, let me try again. Getting close. Okay, I hope that’s visible. First of all, I really appreciate the opportunity to do this. It's an area that I've been involved with for many years now, and I have a fairly strong feelings about ME/CFS. And I hope that the healthcare providers and patients who are listening today will get something out of what I have to say. It’s supposed to move now, right? Okay, good. Alright, let's start with some givens. This is a disease which is clearly exhausting for patients, and it can be challenging for their physicians and other healthcare providers. Which means that many healthcare providers avoid seeing these patients. Uh that's not unique to where I practice, I think that's something I've seen in many other areas of the country.

They're missing out on something, I think. These patients, though we today don't have a cure, they can be managed often managed successfully by sympathetic and skillful clinicians. And the successful management, I think, is really very rewarding. I see patients with other medical problems and I'm not minimizing, giving someone a script to fix their high blood pressure.

Zoom Technical Assistance: Excuse me, Dr. Gluckman I'm sorry I believe you have stopped sharing, could you please re-share your screen?

Dr. Stephen Gluckman: Okay sorry. Let's see I don't know how I managed I don't know I managed to do that, there is that better?
Zoom Technical Assistance: Okay, you can go to display settings and swap your view up in the upper right-hand corner because we’re seeing your notes view.

Dr. Stephen Gluckman: Really? That.

Zoom Technical Assistance: Yep

Dr. Stephen Gluckman: Okay.

Zoom Technical Assistance: We’re still seeing your notes view.

Dr. Stephen Gluckman: I swapped it. Really. I’ll try again. Swap presenter view and slide view. Swapped. No?

Zoom Technical Assistance: Okay, give us one second, we’ll help you out if you stop sharing.

Dr. Stephen Gluckman: Okay. Sure. That I know how to do, sort of.

Zoom Technical Assistance: Standby Dr. Gluckman, we’ll have your slides up in one moment.

Dr. Stephen Gluckman: Okay, no I’m in your hands. Because I don’t know how to do this. As is clearly evident.

Zoom Technical Assistance: We’ve got you covered.

Dr. Stephen Gluckman: Right. Tell me when I should go.

Zoom Technical Assistance: Will do. Here come your slides.

Dr. Stephen Gluckman: Now what?

Zoom Technical Assistance: And when you’re ready to proceed, you can just say next slide, so I believe you stopped on.

Dr. Stephen Gluckman: Slide five.

Zoom Technical Assistance: Okay.

Dr. Stephen Gluckman: Okay. So, when you’re going to move them is that the idea.

Zoom Technical Assistance: Yes, just there we go. And.


Zoom Technical Assistance: Okay, thank you.

Dr. Stephen Gluckman: No, thank you. Alright so. I was sort of commenting on the last moment about successful management being rewarding and then the example I gave was do see uh people with, for instance, high blood pressure and I do get them scripts it takes a high blood pressure, but it’s not nearly as rewarding as managing patient with chronic fatigue syndrome,
we develop a different relationship with them it's much, much, much closer and uh I get a lot a lot more out of it. Next slide please.

Yeah. Good, uh next bullet.

So, some basic tenants of management, uh this is, uh I think we need to educate our patients about diseases that they have in general I think they make for the more they understand the more comfort comfortable they are. This is a disease that clearly mandates educating patients about the nature of this disease. Next bullet.

And another feature that I think is critical is making it clear the patient has come to healthcare worker who completely believes the validity of their symptoms. And I'll comment on this a little more, as I go through this. But most of the people I see have gotten vibes at least from healthcare providers sometimes employers, sometimes friends, sometimes family members that their symptoms aren’t real or valid. Which so not only are they suffering from a debilitating illness, but they’re sort of blamed for it. And a lot of people I see least initially, come with a serious chip on their shoulder they’re determined to prove to me that they're not well and I try to make it clear to them, they don't have to do that I know they’re not well.

Next.

Uh, there are, and I tell people up front, though there's no cure there are ways to manage many of your symptoms, to make you get more out of life with your disability next, please.

So, what is this educational component consist of? So, first of all I make it clear that chronic fatigue syndrome is not the same as chronic fatigue next, please. Next bullet.

Thank you, chronic fatigue, those of you and who see patients know this is, is very common and the something like a third of our patients report, at least on one visit, if not many that they're fatigued and the point prevalence is estimated to be about 5% in studies, though I tell ya if I went around my waiting room I say if I went around my waiting room I think that point prevalence is higher. And I'm not talking about chronic fatigue syndrome I’m talking about patients who say they're fatigued. Next slide please.

This is hard to come by really but the estimated prevalence of chronic fatigue syndrome in the United States is 1 to 2 million and the point prevalence is uh end up well below, well below 1%. Next slide please.

I comment on this several times when I'm seeing a patient. This is the Institute of Medicine now National Academy of Medicine review, which was published uh in the early part of 2015 and it was a comprehensive, comprehensive review and with really unimpeachable, authors.

Next, please.
The original draft was massive. The people on this panel represented all aspects of this disease; scientists, lawyers, academics, lay persons, particularly lay persons with chronic fatigue syndrome.

Next.

It was heavily referenced it was heavily vetted by outside reviewers and public comments. And it there, there are many aspects of it that I think one needs to know about and I lifted some quotes from that IOM review and one of the most important was again, this is a group that really study this they had no agenda, other than to try to be as complete and accurate as possible. One of the quotes I lifted, was that “ME/CFS is a serious chronic, complex, multi system disease and frequently and dramatically limits the activities infected patients. In its most severe form, it can consume their lives. It is real.” This is their conclusion, and it is not appropriate to dismiss these patients. They clearly, again stress the legitimacy. I have a couple of other quotes, sufficient evidence that ME/CFS is a disease with physiologic basis, it's NOT a psychological problem, and it should be taken seriously. Next, please. Next, please.

A second thing they did was sort of what I would consider simplify the diagnostic criteria. Clearly, um I’m on a different page. And I think this is simpler - They basically boil it down to three:

One is fatigue that's a pretty much a given. But it's fatigue that that really gets in the way of things people do either. What happened? Keep going back [advancing slides]. Keep going, there you are, good. Nope, there, good. Nope back thanks. Uh, um, it's not just being tired once in a while. These people, it gets in the way of their work; it gets in the way of their fun; it gets in the way of their social lives and these by this definition has to persist for six months, or more, I will comment on that in a second.

A second of the three major criteria is post exertional malaise. Exertion is sort of an expanded in that that doesn't have to be physical exertion. It can be, it can be psychological exertion; it can be you know working at work and using your brain and it can be motional, emotional exertion stresses any of those things people with chronic fatigue [syndrome] are particularly susceptible to making it worse and typically it's not immediately it's like the day after they have a setback. Day after they've had some sort of stressor. And the third component is unrefreshing sleep. They get up in the morning, they don't feel refreshed.

The other two components that they suggest is cognitive impairment and I cannot tell you how many patients use the words brain fog and orthostatic intolerance. Next, please.

There are many other symptoms that one might see in patients who have chronic fatigue [syndrome], and this is not a complete list, but it gives you some examples of some of the things and I'm not going to read it.

Next, please.
Uh this confuses some patients; I often usually comment on it and uh when I tell this is more my belief and I'm not sure it's universally accepted, that for me there's a continuum between a diagnosis of fibromyalgia and a diagnosis of ME/CFS. Some people are way on the pain end and those are the people that get labeled as fibromyalgia some people are way on the fatigue end and that's the typical patient with chronic fatigue syndrome, but many patients have a mixture of symptoms that people with that they get called chronic fatigue [syndrome] do have some often have elements of pain um and other features of fibromyalgia.

The many patients with ME/CFS have issues with their autonomic nervous system, often most commonly manifested as orthostatic hypertension or POTS. And there's a subset, I don't see this as much anymore, that are called CFIDS which is chronic fatigue and immune dysfunction syndrome and I underscore dysfunction that's not deficiency. People with chronic fatigue syndrome are not particularly predisposed to opportunistic infections like we might see in a person with advanced HIV they don't get pneumocystis they don't get cryptococcal meningitis. But there are aspects of their immune system when you when measured in the laboratory are not normal so it's somewhat dysfunctional but not deficient. And so, some people get labeled CFIDS, again I haven’t seen that term use nearly as much as it used to be.

So, having said that, and that's the official definition, it's important understand case definitions. Case definitions are used when we don't have a definitive diagnostic test it's not unique to ME/CFS. If you had any one of 12 opportunistic infections between 1980 and 1985 or so you were diagnosed with what we now call HIV, whether you actually had it or not. If you were in the Bellevue-Stratford Hotel in Philadelphia in July 4th, 1976 got pneumonia you were diagnosed with Legionnaires disease, whether you actually had it or not. So, these case definitions are research tools they're epidemiological tools and they’re useful clinical tools, but they're not absolute. As an example, if somebody had obviously to me has the features of chronic fatigue syndrome, but it's only been four months, I don't tell them come back in two months, I'll tell you what your diagnosis is. I'm comfortable telling them, you have chronic fatigue syndrome, even though you don't completely fit the present-day definition. Next, please.

So. Um it is complicated it is somewhat controversial but less so, and I suspect there, there are people on this today, who would have arguments with many of the things I’m going to say, that's the nature of this disease as we learn more and more about it. But having said that, it's important to know and to stress to the patient that it's not new. It is real as I've said, and we actually do know a great deal about it because it's not new. I can tell a patient with confidence that they're not going to develop liver failure from this or kidney failure from this they're not going to die of this. They are likely going to suffer and because it's not new I can say that it's not going to go away in the next week or two weeks or a month, but this is a long-term illness with waxing and waning features. All that I can tell people confidently because it's really not new.

I feel strongly about the next bullet point, which is that I'm not insisting that a healthcare provider believes in this disease even, although I think they're wrong if they don’t. But I do
insist that those people that that doubt the validity of this disease or the patient's symptoms can't effectively manage these patients and they just should defer to somebody who is more comfortable managing them. Next, please.

So, it's not new and I explain this to patients, it's just relatively newly named. Next, please.

So, I give them a couple of examples, I just threw some stuff up here, I say, if you came in here in 1880, I would have said, we have classic neurasthenia because that's what it was called then it was named by a neurologist named Beard, it was it was based on some theories which didn't hold up. But it there's an interesting quote in Osler's textbook from around that time quote, “in all forms there is a striking lack of accordance between symptoms of which the patients complain and the objective changes discoverable by the physician.” That sounds to me like ME/CFS.

If you came into this office in in the 1950s, I would have said right, you have chronic brucellosis because that was based on...brucella as most of you know is a real bacteria and we can get infected with it, but there were some lab errors that suggested that that there was a disease of chronic brucellosis that was responsible for this and that's been pretty much not pretty much it's just been retracted I don't see anybody have chronic brucellosis.

Somewhat analogous, however, in 1985 was a publication in the annals of internal medicine, suggesting that this disease was due to chronic Epstein-Barr virus. That also has been disproven completely, there is no such disease, though this is not completely vanished, and I do see occasionally people with who've been told they have it and that's really due to a lack of understanding of how to interpret the serology. Many other things have been proposed, all of those other things listed have, for one reason or another, been disproven. But again, the idea is it's been around a long time. Next, please.

Thank you. So, summarizing a little bit for patients, and I do this for patients about what we know about etiologies again. The bottom line is we don't know the cause. Many infectious agents have been proposed, none have been found and specifically linked causally to ME/CFS. And so, at the moment there's no evidence that this is that the symptoms are due directly to an active pathogen. There are variable changes, one can find in a number of different hormones, but none of these are profound enough to explain the entire syndrome, though they may have some role in some of the management or affecting them may have some role in the management. I've already commented on immune problems, people have looked for the standard issues with autoimmune problems and, though, again, you can find some abnormalities none of them are profound enough to explain this syndrome. None of the things that we usually look for we're looking for you in problems and, as I emphasized, and I will again, they are not immunosuppressed. Next please.

It may very well turnout, and this is not my unique thinking at all, that that this idea of looking for a single cause is fundamentally flawed. That there may not be a single cause and there may be a number of different events that can initiate this and that you have to have a certain
makeup genetic or chemokine or some other underlying makeup it then triggers the ME/CFS. So it may be that there isn't one cause and looking for one cause will never be successful.

Next, please.

So, again I emphasized patients and healthcare providers if they're somewhat skeptical it is in fact a biological illness it's, it's fundamentally not a psychological disorder, though there are some psychological issues that can come up. One of the things that's clear and those of you that that that care for patients, I think you understand this easily that these are not malingerers, they want their prior lives back their prior usually very active lives back, they’re not faking something to get out of work, they want to work. They want to go back to their triathlons or whatever active things they were doing. They're not hypochondriacs they didn't spend their adult life in and out of health care providers offices with one complaint or another, these were highly functioning people. And as I've already mentioned, you can find multiple and more and more studies are showing these multiple pathophysiological changes and abnormalities in immune system and cellular metabolism, neuroendocrine system, autonomic nervous system, so there's stuff going on and just because we don't fully understand it, one shouldn't take the easy way out and call it just in their heads, just a psychiatric illness.

Next, please.

I point this out also it, it is a more accepted illness than it was when I first started. When I first started, those of you that doing this for a while recognize this, I'm sure, if somebody needed disability insurance, it was a serious project to get it 20 years ago and required multiple letters and yelling at the appropriate people. Now it's much more sort of standardized, there's uh even an ICD 10 code for it. So, it's a little easier, but these problems have not completely gone away, certainly the disability insurance problems. Next slide, please.

So, how can we diagnose something without a diagnostic test? I'll tell you what Osler did, and our medical forbearers did, and you can. There is a characteristic history, and this is usually again history not associated with malingering or hypochondriasis these were highly functioning people that want their lives back. There is a characteristic physical exam, which is, in fact, in terms of the standard stuff we do normal if it isn't that has to be worked up. If somebody has a large lymph node you don’t call them chronic fatigue syndrome. You evaluate them to see why they have a big lymph node. And there are characteristic lab tests and by this I’m talking about standard lab tests, not research lab tests. And if somebody has a high white [blood cell] count, that that needs to be evaluated, that's not what you see in chronic fatigue syndrome. If they have thyroid abnormalities that's not chronic fatigue syndrome. Next, please. Keep going, sorry. Yeah, this coordination is a little complicated.

I've said this, that the pre CFS history [oh back one slide, please] is NOT one of multiple somatic complaints. They contacted or contracted some stressor and they basically, that often goes away, it can be triggered by something as mundane as a standard infection. But that goes away and or in the case of Long COVID, which is probably one of the triggers uh COVID is probably
one of the triggers. There's no active infection anymore, but it has triggered this syndrome, which we now call ME/CFS. Next, please.

So, one of the features, I think that's important when you're managing these patients is, be particularly type A about history and physical. You want to make sure they get the message loud and clear that you are taking this very seriously, even if you know the diagnosis in five minutes. And so, I do MMSE exams simple fast, I do it for two reasons, in addition to the usual standard complete physical, which I'm very careful about how I look at their fundi, etc. I do it because it's some sort of objective measure to follow, but more importantly because most people I see have never had anything like that done, and again in doing it patients getting the message I'm taking this really seriously. Next, please.

So, a couple of specific points to emphasize patients often complain of fever, but very few have significantly elevated fevers if they do, they need a work-up. If their temperature is 102, that's not chronic fatigue [syndrome]. Many of you in the clinical arena know uh all the patients that say I run low temperatures normally I don't get into a debate with them about that. Uh, as you know, many of us are in the 97s, that's normal. At least for parts of the day.

Joints ache but there's no objective evidence if somebody has a fluid filled joint you work it up that's not chronic fatigue syndrome. It may be another problem in a person who has chronic fatigue syndrome but that's not the cause, that's not chronic fatigue [syndrome].

The fatiguing if you did objective testing and they're not done much anymore, because they're mildly invasive like EMGs and muscle biopsies, they're normal. If they're not normal you got it if somebody has an abnormal EMG, you got to figure out why.

Lymphadenia, people say the lymph nodes are enlarged, but if you then go on and examine them and discuss it with them it's more that they feel them they're prominent they have lymphadenia. If they have a large lymph node, you work it up. Next, please.

Those that know me know I'm a real nihilist about testing in general and I don't do a lot of tests, because of my concerns about if the pretest probability is low, my positive test is going to be a false positive and that gets people confused. So, my usual testing and again I, this is not in a research setting this is clinical practice, is a CBC chemistry screen TSH. And I have a fairly low threshold for cortrosyn stim because I never want to miss adrenal insufficiency and for sleep studies, but I that's about it. Next, please.

I don't routinely do these serologies. I think not only do patients not understand them many doctors don't understand. Serology is rarely a diagnostic test and I explain this to people somebody comes in with positive Lyme serology and I explained it to them it's pretty meaningless. For instance, if I test your blood today for antibodies for serology to chicken pox, I'm going to find antibodies, you're an adult either you were vaccinated or you had the disease. But are we going to have to spend a lot of time discussing why you're not suffering from chronic
chicken pox? So, the fact that you find antibodies in somebody's blood doesn't tell you anything about activity of the disease and it can just become confusing.

Similarly, with ANAs, people with chronic fatigue syndrome have none of the criteria for lupus, zero. But if you do an ANA and it turns out to be 1:40 you've created a really slippery slope. They'll Google it, they'll get involved in all sorts of other unnecessary tests, I don't do it.

I don't do expensive neuroimaging, same reason I've already said I'm pretty slow to do any testing, I'm one extreme, I understand that. If somebody has objective neurological things of course I'm going to do neuroimaging but otherwise, many of us have UBOs, sorry to tell you this, in our MRI, unidentified bright objects, that's going to confuse people.

Tilt table testing I do occasionally but rarely because I don't think it's going to change the way I manage the patient. If they have symptoms consistent with POTS or other orthostatic hypotension, I'm going to treat them. And so, I tend not to do tilt table testing, but I do occasionally, and I know a lot of people do it. Next, please.

So, in answer to the question, can you make a diagnosis on somebody without giving them a positive lab slip your ME/CFS titer is X, or you have a diagnosis, yeah if they have a typical story, they have a negative physical and they have negative screening tests, I think you can make the diagnosis. And I do. Next, please.

Alright, moving then on to other aspects of successful management. All the things I've said, not only is potential education for healthcare providers, I think patients need to understand all that. And I spent a lot of time, which is probably one of the other reasons many of my colleagues don't want to see these patients, they do take time to do it right, and if you're not going to do it right you don't do it. Next, please.

Oh, you did it already. So yeah, patients with ME/CFS are partially or completely disabled one of their problems, and problems of course it's in quotes, this disability is usually invisible and that's makes it more complicated for them. Next, please.

Oh wait, you're already one ahead of me, sorry. The outward they look okay and they're testing is okay, they just they don't feel okay, if they were unfortunate enough to be in an accident or paraplegic, they wouldn't be dealing with justifying their disability they wouldn't be getting the negative vibes that they might get. Well, these people are, can be as disabled but because it's sort of invisible they're often dealing with a lot of negative vibes. And hence, they get, it's common for people around them to not believe that their illness is real or valid and not only are they suffering, but they're sort of blamed for it, so they're hit doubly. Next.

So, a lot of people I see come in with a fairly sizable chip on their shoulder there, because they've got these vibes from other health care providers, and I just tell them up as best I can up front that I know their illnesses real, let's get past this in this office, I believe you. Let's get past it, let's talk about this disease and about what options you have for improving your situation. Next please.
And those again of you in clinical practice understand, in for all illness but particularly in an illness like this, that our support and our understanding is really a critical part of good clinical care. Next, please. Next, please.

So, you got to give them enough time as I say, even if you know what they haven't five minutes you got to make sure they know you're being very, very thorough, because ultimately your diagnosis is based not on a lab slip but on your opinion.

Next, please.

Go to that I've said that several times. Next please. I specifically discuss with them problems they might be having in dealing with the validity of his or her disease, not only that they start to question it, but of course they get questioning from everybody around them. Next, please.

And again, as I said, and I can't really, I can't overstate it, don't underestimate what a clinician can do with trust and support and reassurance. Patients get a lot of therapy out of finding somebody with an answer, who believes them. Next, please.

And I do go through, in some details of the history that it really isn't a new disease we know a lot about it, which means I can prognosticate, as I mentioned, they don't get liver failure, they don't die, and also prognosticate in the sense that this is going to be a long-term problem with fluctuations. Next please. Next, please.

I don't get I don't debate at all, about the issue, whether this is primarily psychogenic, remember psychogenic illnesses are real, but I don't get into that or organic I think that's just opening up a can of worms and patients somehow or other often just hear, he thinks it's in my head and they shut down. Next, please.

So, a few more specific steps like I do make it clear that there is no cure. If there was a cure, they probably wouldn't be sitting in front of me now. But there are treatments that can improve their situation. Next, please. Next, please.

I think it's important that we reframe their expectations. They have a disabling illness; they can't do what they want to do; they can't do what they were able to do prior to getting this illness. Which is no different than if they were hit by a truck and uh paralyzed. But, again, because it's less visible it's harder for people to accept that. So, they have to have, thanks that's good, they to have those expectations, and they should try to focus on what they can do, even if it's quite limited, rather than lament what they can no longer do. Because they can't do it it's just going to torture themselves. And by focusing on what you can do you may be able to get more production out of that limited period of time.

So, what else, more specifically. Well, this is totally controversial, I understand that. But I am one of those that is a believer in exercise. But it just has to be done very, very gradually because they are very susceptible to setbacks, and they want their lives back, their active lives back and they unless you're really rein them in, they're going to overdo it, and have a setback. So, I
prescribe what I, in discussing with them what I believe is something that they can definitely do without a setback, and for some people that's getting dressed; for other people that's walking to the corner. But I want, but I think it's certainly good psychologically to get up and do something and uh and I think sitting is in itself somewhat fatiguing. This is controversial and I again I underscore that that you have to be very clear that it's got to be very gradual and very little to start with, and then possibly nudging it up.

CBT, little bit controversial too but to me less so. It certainly doesn't help everybody, but some people who have symptoms that are otherwise unfixable do get some benefit out of CBT. It certainly doesn't have side effects so taking medications either prescribed or complementary therapies, of one sort or another have potential for side effects. You do not get diarrhea from CBT you do not get rashes from CBT you don't get liver injuries from CBT, so I suggest people give it a try. Next, please.

So, having said that, I avoid the discussion of psychological versus organic cause. I do tell people that it's hard to imagine that somebody whose life is this uh impaired isn't depressed. Which is no different than if you had bad rheumatoid arthritis and couldn't use your hands very well, you should be depressed, and I have good news for you that there is medicine to treat depression, it doesn't treat chronic fatigue syndrome. But if your depression is aggressively managed it will help you cope better with your disability. Most people with chronic fatigue syndrome are highly susceptible to medications, they don't do well, so I do treat depression, but I start with very, very low doses, get them adjusted to it and then gradually increase it. Next, please. Next, please.

Sleep is an issue. If we are sleep deprived all symptoms are worse, so I aggressively try to help manage sleep, occasionally, with the help of a sleep specialist. Next.

I treat other treatable conditions, this is sort of obvious, but I want to make sure they understand that that having ME/CFS doesn't mean they can't get other things. And one shouldn't assume that every symptom they have, from now on is ME/CFS related. I mean a ridiculous example if they got a urinary tract infection, I treat it. So just be careful not, attributing everything to ME/CFS. Next, please.

Pain, some people have a lot of pain some people have no pain, many things have been tried. The traditional drugs for pain, at least for the for fibromyalgia, amitriptyline and, or personal treatments I should say, and physical therapy. But all of these things are tried there's been no head-to-head trials, of which is the best management option and it's a trial-and-error thing. Again, remembering people are highly, highly susceptible to medication side effects, with this with ME/CFS so you got to start really, really low. I happen to like amitriptyline because it has a side effect of potentially helping sleep. Next, please.

The fatigue itself, there's strategies. That, uh basically, the idea is to try whatever time you have during the day that you think you can use, and that may be an hour or two hours compared to the 12 hours you used to work. Uh try to figure out ways to use that effectively and doing
something that you find worthwhile and gratifying. It may be something you've never tried before. But there's there are potentially many options. Take more breaks, mindfulness and stress reduction there's no side effects, I like it as a thing to do, in general. If you're if you haven't if you are able to work enough and have an understanding employer, try to get some accommodations at work. Work half days, work partially from home, get permission to take a break in the afternoon, something like that. There are medicines that will in many people improve fatigue, I do prescribe these, but I don't prescribe them for everybody. Those in clinical practice understand that these have potential problematic issues, but I do prescribe them, in the minority of patients.

Almost done. Orthostatic intolerance. If they have symptoms of orthostatic intolerance again, I generally don't put them through a tilt table test - I treat them. And support stockings, ideally these should be fitted support stockings and waist high, and there not so easy to get into not so comfortable but they're the best. And they these this group people, unlike most of us, can increase their sodium intake. There are some medicines, which again are potentially beneficial, you got it's a trial-and-error thing to help ameliorate some of the orthostatic symptoms.

Cognitive problems, this is brain fog, it's a matter of being organized. And setting up routines using aids like smartphone reminders or habit stacking to try to compensate for some of your memory and other cognitive disability.

Finally, I see them at regular intervals, I don't want to, this is not unique to this people with chronic problems, you don't want them to only call you when there's an urgent issue. So, they know they have a scheduled appointment I seen them at regular intervals, that's generally three months. But I have a discussion with them after a while, you think, you think this is the right thing for you, if you if you want to be seen less frequently and let's make it every six or annually. If you need to be seen weekly, ain’t happening. Then you, then you do need a shrink. I don’t tell them that.

Many of our patients, not just chronic fatigue patient, take many drugs that we don't prescribe. And that's a discussion that happens with every new patient I see, even if they're coming in for unrelated for non-ME/CFS problems. And I just caution them that, though you can get them they aren't proven in terms of efficacy and unproven in many cases in terms of, of side effects. And this whole idea of organic is particularly problematic to me, arsenic is organic I don't think I would prescribe arsenic for them. So, my deal is this, and I tell a patient straight out, you're an adult you absolutely can do what you want, you win so I'm not going to fight with you about it, but I'd like to know what you are taking because I'd like to give you my thoughts on it, particularly if I think it's potentially dangerous or very expensive. But do not fear, I will not fight with you. I offer them the CDC website, which was mentioned at the beginning of this, I suggest if they don't read the IOM report that maybe people around them should, so they’ll get a little better understanding from family and friends about the validity and legitimacy of this illness.
This is a list of some of the things that have been unproven and done, I point out one, because I think it's interesting. So, many years ago, Acyclovir was studied, though of course there's no evidence this is viral and certainly no evidence that Acyclovir, which is really for certain a few herpes viruses, would have any particular benefit. And interesting enough about 70% of people improved at least transiently, however, more interestingly about 70% of people within the placebo group improved. So, I would be cautious about uh anything people are using that's been studied, but not studied in a strict fashion by good double blind controlled trials. They can take these medicines, of course, but I would be cautious, because some of them have potential downsides. Certainly, interferon does, antibiotics do, steroids too so, I caution them.

Finally, like all the patients, we see, we need to accept the fact that we won't always be successful but that doesn't mean we should default to the temptation of unnecessary and potentially dangerous treatments like prolonged antibiotics. They have certainly negative consequences.

Thank you very much, I hope this didn’t sound too much like a sermon and I’m happy to address questions or concerns or arguments.

Kate Fowlie: All right, thank you very much for that presentation, Dr. Gluckman. We will now move onto the Q&A a portion of the call. There are four ways to ask a question. If you're joining us via Zoom you can click the Raise Hand button under the webinar controls on the bottom of your screen. If you can't find the button, or it won't work for some reason, you can type your question into the Q&A box. And if you're joining by phone, you can enter *9 on your phone to join the question queue. Um and when you we announce it's your turn to actually ask a question, you can press *6 to unmute yourself. Lastly, we have the ME/CFS email address, which is mecfssec@cdc.gov that will be the slowest option. And we've already received quite a few questions from you in the in the Q&A box so we'll just dive into those right away, and we will try to answer as many questions as possible, uh we may not be able to get to all of them.

The first two are for Dr. Unger. Dr. Unger you mentioned phenotyping in the COVID UPP study, will this phenotyping involve CD16 positive or CD56 bright.

Dr. Elizabeth Unger: Uh that's a very detailed question. The PI in this is Dr. Nancy Klimas and she has studied NK cells, those are markers for NK cells, I believe she'll be doing flow cytometry but I'm not 100%. She has selected specific measures of natural killer cell functions that she feels are most important for uh ME/CFS that will be done in comparison to the Long COVID.

Kate Fowlie: Thank you. And also, Dr. Unger, you mentioned several papers in the MCAM study, are those papers available in pre-print.

Dr. Elizabeth Unger: The papers that are published are available in you know, through PubMed. And so, they aren't preprints and the other ones aren't yet and aren't yet uh published so they aren't available, we're working on them.
Kate Fowlie: Alright, thank you. The next question is what steps will the COVID RELIEF take to deal with the issues with current coding of ME/CFS, where ME/CFS uses the same code as the symptom of unspecified chronic fatigue?

Dr. Elizabeth Unger: Right and all studies relying on medical record healthcare medical record and ICD coding are very challenging in ME/CFS and that's because the codes are confusing, and the clinicians don't code accurately and so that's a limitation that we always need to do the best we can. In COVID RELIEF, we aren't focusing so much on ME/CFS we are going for the symptoms and the new diagnoses. But um coding, and even the coding of Post COVID Conditions, there's a new code for that. We need to really work on improving that to make our medical records much more useful for surveillance of ME/CFS and other complex chronic conditions that are challenging.

Kate Fowlie: Okay, thank you. And the next question is this is both for both of you, Dr. Unger and Dr. Gluckman, do you have any trials for patient-initiated treatments, could you please consider a compassionate use type of program to free doctors to treat patients with therapies that apparently work.

Dr. Elizabeth Unger: I can't, CDC is not responsible for the clinical trial so I'm sorry I can't really respond to that. That's an FDA decision about uh compassionate use of drugs, and I don't know Dr. Gluckman do you have some additional comments.

Dr. Stephen Gluckman: No, No I don't I also don't have any clinical trials. Um and I would be cautious about quote apparently work unquote. As I've said, if people have access to these things, they're adults, they can take them. But I would be cautious about anything. Maybe I'm just too old fashioned, but I'm paused by anything that hasn't been shown to work in a good study because drugs have side effects.

Kate Fowlie: Okay, thank you both. The next question is, could you please baseline how much care time it takes to appropriately care for a CFS ME patient, and this would level, this would level set expectations on both sides, and someone talks about their personal experience as both the clinician and patient that it takes weekly 30-minute sessions to fully address this multi system complex illness.

Dr. Stephen Gluckman: I think it takes more than 30 minutes. Initially it takes between an hour and a half and a sizable chunk of that is, if not all of it is educational, well there's a good physical in there, too, I should say. Maybe in my youth I could have done it, but my administrative assistant knows, not to schedule a new patient with potentially this diagnosis, more than one a day. I think follow ups can be done in a much shorter period of time and not five minutes, but more like 20 to 30. But the first visit is a long visit.

Kate Fowlie: Okay, thank you very much. The next question is for disability applications patients need objective numbers, such as provided by tilt table testing, how are patients supposed to proceed?
Dr. Stephen Gluckman: Me? Well, my experience is they don't necessarily and again I've done this, a lot, and most of them most of the disability forms I've filled out don't specifically need that. If they need those things, it's clear they do, I do them of course. Occasionally, I need to get you know some of these forms want can they lift five pounds, 10 pounds, 15 pounds; those sort of things, that that's not my area of expertise I'm a mere internist and infectious disease doctor and I will send them to a physiatrist, say, please take care of this part of the form for me.

Kate Fowlie: Okay, thank you very much. Someone asked if there be a recording of this available later, and the answer to that is yes. We will go ahead and take some of the calls, questions from people who have raised their hands. Let's go ahead and start with Hanna Ward. And I'll go ahead and please unmute.

Hanna Ward: Thank you. Thank you, can you hear me.

Kate Fowlie: Yes, we can hear you Thank you.

Hanna Ward: Oh, thank you, my question is for Dr. Unger. When the CDC speaks to the ME Community CDC leaders tell us what they're doing but they don't speak bout measurable outcomes that directly impact people living with ME. Dr. Unger, people with ME do not care about the number of page views, something has gotten, just to be completely transparent about this. Please understand that people within ME care about actual improvements that we need to experience with clinicians, insurance companies, accuracies of articles and op eds that are published about ME and so on. But CDC does not talk about results of its efforts and by results, I mean direct measurable impacts of its work and whether or not its efforts have actually reduced the suffering and risks of harm to Americans living within ME, this is what matters to us. For years, when members of the ME Community have spoken with the CDC and shared that stigma against ME has continued unabated, CDC always replies by describing things how things should be and not how things actually are, this is grossly unacceptable, and it is a clear example of CDC’s denial and gaslighting. The CDC must stop this practice in doing so, CDC denies facts into a nice reality. This kind of conduct by a taxpayer funded federal agency is not what Americans require of the CDC. We demand that CDC stop playing politics at the cost of our lives and as an act of integrity and goodwill, publish a statement on the CDC’s ME/CFS homepage stating that ME/CFS is neither psychological nor psychiatric. Any indirect language or actions will remain unacceptable. I look forward to you treating us with respect, thank you.

Dr. Unger: Oh, thank you for your comments, our web page does say that ME/CFS is a biological illness and it's not psychological. And I apologize, that our measures are indirect you're absolutely correct our end goal is to increase the number of healthcare providers that understand ME/CFS, and at this point our indication is just who is using it, so I understand your comment, thank you. And Kate you’re mute.

Kate Fowlie: Thank you, excuse me for that technical problems. Just moving to the next person who raised their hand if we could go ahead and do, that Amanda I'm going to go ahead and ask you to unmute please.
Amanda Mathiesen: Yes. Thank you. Can you hear me?

Kate Fowlie: Yes, we can thank you.

Amanda Mathiesen: Excellent. I'm a former marathon runner who has CFS/ME. The CDC and the World Health Organizations have removed graded exercise therapy from their recommendations for people with ME/CFS. And in the UK, the National Institute for Health and Care Excellence says don't offer people with ME/CFS any program that uses fixed incremental increases in exercise, for example, graded exercise therapy. So, what I'd like to know is what is the CDC doing to promote up to date treatments and discourage doctors from recommending interventions that have been proven detrimental, such as the graded exercise therapy that was recommended to me by a very nice and well-meaning doctor this year.

Dr. Elizabeth Unger: Thank you for that comment. CDC does not use the term graded exercise therapy. I think that the, the key word there is incremental and um and continual. The balance between maintaining activities that are tolerated versus going on a fitness campaign is just needs to be kept in mind. So, because of that, we do recommend pacing on our website, which is the process of trying to manage the activities of the day within what's perceived as the energy envelope, or something like that, so that pacing allows the patient to optimize their activities throughout the day and to the point to avoid the over exertion that results in the post-exertional malaise, or sometimes called a crash.

Kate Fowlie: All right, thank you. Another question I believe is for Dr. Gluckman. Do you know of any studies investigating the micro dosing of psilocybin and or ketamine to treat energy, brain fog, depression and pain?

Dr. Stephen Gluckman: Both of us let's start with that. No, I don't know of any studies that I would call um meet, uh you know what I think most people would say is accepted criteria in terms of good double blind controlled trials. As I gave that one example, with the Acyclovir. Yeah, you need double blind trials and because, again the Acyclovir looked good until you compared it to placebo. And these drugs do have potential for side effects, so I'd be cautious.

Kate Fowlie: Thank you for that answer. We'll go back to the hands raised. Um, Alex if you could unmute yourself.

Alex T.: Hi, thank you, can you hear me.

All: Yes.

Alex T.: Sorry, I cannot remember the names of the various doctors, but this is directed to our guest speaker. I just was wondering, so I noticed in your presentation, you were saying that the use of corticosteroids may is not recommended for joint pain. Now for myself as a patient the only thing that has helped with the severe joint pain has been prednisone. I don't take it ongoing but just at times when the pain it's for many days and it's very intense. I'm just wondering if you will have recommendations on studies or research that will address this topic.
Dr. Stephen Gluckman: Well, specifically corticosteroids sure. First of all, anytime we take a medication, we are saying, if not out loud, we’re saying to ourselves, we think that the uh potential benefits outweigh the risks. Every drug has a risk. Certainly, steroids have risks. So, if that's if that's what you need to do to function, then I you say I'm going to do this and I'm going to accept the risks. I have no argument with that at all. But I do caution people that, particularly in this case steroids, that they have potential side effects, so I tell them to take as little as you can get away with as infrequently, as you can get away with it, but I don't have an argument with if that's if that's what you need to function, then you then you do it. It's no different than taking any other medicine. Every drug has side effects.

Kate Fowlie: Thank you, Dr. Gluckman. I will take another caller, and this ends with 082, I apologize I don't see a name, if you could unmute yourself. If you're able to, 082 if you're able to unmute yourself. If I will come back to you. We have time just for a couple more questions. I have a question here, that is for Dr. Gluckman. What advice would you offer to a patient who has seen dozens of clinicians who admit, they just don't understand enough about ME/CFS to treat me, those doctors are specialists. And they will routinely, you know that the doctors who are specialists routinely have really long wait lists. What would you say most doctors’ offices knowledgeable about this say they’re not seeing patients? I've even tried to see other doctors. It can be frustrating, what would you what would you say?

Dr. Stephen Gluckman: Well, the real answer is, I don't have a good answer, other than to say what I said and what is implied in the question, I think you need to see somebody who understands this disease or is willing to at least learn about this disease. Because it’s much more critical than, again anybody can look up how to treat high blood pressure, this is way more complex than that. So yes, you need to somebody who, who is willing to understand this disease and has some understanding of how uh disabled people can be. Having said that, I mentioned at the beginning of my discussion that it's hard to find those people. Most of my colleagues, I'm in a division with dozens of colleagues, nobody else wants to see these patients, despite the fact that I try to tell them how rewarding it is. It does take a lot of time and you have to be willing, and a lot of emotional investment, and for obvious reasons most of my colleagues, if not all of them here, are not interested in doing that. I think it's hard to find good clinicians, I don't have a good answer I'm sorry. Get on a waiting list.

Kate Fowlie: Thank you, Dr. Gluckman. And we have a question here that says can have surgery cause a flare?

Dr. Stephen Gluckman: Yeah. Absolutely.

Kate Fowlie: Okay. All right, one last question is, do you believe that ME/CFS is genetic?

Dr. Stephen Gluckman: Well, it's not, if it's genetic the genetics haven't been solved yet. Because it's not if you look at family if you look at families you don't see a pattern consistent with a specific inheritance. So that isn't to say it's not genetic and it may be that it requires not it's, not a single gene mutation, it probably isn't, of course, but may require some mix of genes
that if you happen to have it, you are now predisposed if you get a certain stressor. So, I think that's still out as to whether there's a genetic component, but there's no obvious standard one because, again, you don't see it in most patients it doesn't run in families.

Kate Fowlie: Okay, thank you, Dr. Gluckman. And thank you to everyone for taking the time to join us this afternoon. We hope you leave us with a better sense of CDC’s commitment to ME/CFS. On behalf of the entire program, we wish you the best over the spring and summer months and look forward to our next call. This concludes today's call. Thank you.

Dr. Elizabeth Unger: Thank you.

Dr. Stephen Gluckman: Thanks, I appreciate the opportunity.