**2nd Interagency ME/CFS Working Group Meeting, February 25, 2021**

**CDC and NIH**

**Day 1 of 2**

*Dr. Inger Damon:* I'm Inger Damon and on behalf of CDC I want to welcome everyone to the second meeting of the Interagency ME/CFS workgroup. For those of you who don't know me, I'm director of the Division of High Consequence Pathogens and Pathology at the Centers for Disease Control Prevention, home of CDCs ME/CFS Program in the Chronic Viral Disease Branch. CDC and NIH brought this group together to create a forum to share information across multiple federal agencies. The agencies represented here report research on ME/CFS and have an interest in issues that impact the lives of individuals with ME/CFS.

Depending on the topic, we also invite participants from patient advocacy groups and patients themselves to share information how to further research on ME/CFS. Based on the Federal Advisory Committee Act, this working group is not considered a federal advisory committee and therefore cannot make recommendations to the agencies involved. The working group can identify opportunities to increase our knowledge of ME/CFS and ways to find solutions to help individuals effected by this terrible disease.

The goal of this working group is to increase communication and collaboration amongst federal agencies and list stakeholders. The agency will provide brief updates on the related efforts and will focus on the specific topic to advance their program's ME/CFS activities. To insure we're meeting the goals of this community, it's important that we share from those most effected by ME/CFS and get input and feedback. So, we'll provide time during these meetings for us to respond to questions that come in from the community. I've been director of this division since 2014. And I've been a member of this division since I came to CDC in 1999.

Several scientists from my division in the Office of Director have participated in various ME/CFS workgroups, discussion groups, and federal advisory committees in the past. We're excited to engage in this effort to continue to discuss what is going on across the

agencies and how we use government scientists to help support the science moving forward to understand the disease, how to diagnose it, how to treat it, and perhaps even how to prevent it. I'm happy to so serve as chair as the group along with Dr. Walter Koroshetz from NIH and I'd like to thank Doctors Unger and Whittemore for their work in organizing this meeting. And I'd especially like to thank those who are participating today and look forward to the discussions throughout this afternoon and tomorrow afternoon.

The goal of today's meeting is to discuss ME/CFS workforce development, documentation of the need, the challenges, and the clinical, and the clinician's viewpoint, and the current initiatives that address that need. The goal of tomorrow's meeting is to update the community on research activities and cross agency collaborations for long COVID.

The federal agencies participating include the National Institutes of Health, Social Security Administration, Veterans Affairs, Department of Defense's Congregationally directed Medical Research Program, Centers for Medicaid and Medicare and Medicaid services, and CDC. We welcome participation of several guests including representatives from Massachusetts ME/CFS and FM Association, and the Action New Jersey ME/CFS Association, Solve ME/CFS Initiative, and presentations from the National Association of School Nurses, Quinnipiac University, ME/CFS Clinician Coalition, NOVA Southeastern University, and the Long COVID Alliance.

We'll use the start of each session for introduction of speakers. After the discussions, at the end of each session, we'll take questions from listeners. If you'd like to ask a question, please click on the Q and A button and type your question in the box then click Submit. We'll read out the questions and panelists will answer them. We'll prioritize questions related to the days topic and hope to answer as many as possible during the meetings. If you have any technical issues, please type your issue in the chat box for help and Monica will provide assistance. A recording of the meeting, along with the agenda and list of participants will be posted to the ME/CFS website after the conclusion of the meeting. With that, I'll turn it over to Dr. Koroshetz from the NIH for some additional introductory remarks. Dr. Koroshetz.

*Dr. Walter Koroshetz*: Thank you very much. Can you hear me all right?

*Dr. Inger Damon:* Yes.

*Dr. Walter Koroshetz:* Great. I want to thank everyone for joining us today. And thank you Dr. Damon and the CDC for hosting this important meeting. We'd first like to welcome Dr. Katherine Argue who is the new representative from the Department of Defense's Congregational Directed Medical Research Program. She is currently managing the ME/CFS Awards under the Peer Review Medical Research Program, so welcome Katherine.

We received a lot of positive feedback following the first working group meeting. And we think this is a really useful venue to help us increase collaboration among the federal agencies and to hear from stakeholders interested in ME/CFS research going forward. We also want to take a moment to thank the patient advocacy groups who've agreed to participate in the meeting. The groups work together with lots of folks, and we look forward to hearing their presentations today and tomorrow on these important issues. We appreciate the group's participation and the essential patient perspective that they bring to the meeting. It's all about trying to get relief for people who are suffering.

And we're also aware the main topic of this meeting is trying to see what can be done about improving healthcare for people suffering with ME/CFS, particularly around the issue of expertise and interest of healthcare providers with experience and expertise in ME/CFS. It's a critical topic for discussion with this group, we're excited to hear your ideas.

Later this afternoon, Dr. Vicky Whittemore will speak to you about training awards, trying to get young people interested in ME/CFS through research and fellowship, research fellowship opportunities supported by NIH. Clearly that's just a small piece of what's needed which is much more awareness and interest on the part of primary care physicians and different specialists taking care of folks. And so, we're looking forward to the meeting and I'd like to turn it back now to Dr. Damon.

*Dr. Elizabeth Unger:* Actually, probably I'll, this is Beth Unger, yeah. And I'll start off this session and try to explain the way we've organized this agenda. We asked the, several

of the patient advocacy groups to work together to give a presentation to set the stage for the need for healthcare and the need for workforce development. And, then we will move to the challenges that are faced by clinicians trying to meet that need. And, then we'll have a break and then we'll talk about some initiatives that are and have been done to try and address this. And, then we'll have a bigger discussion about how we can move forward. And, then we have a small amount of other business.

So, for our first presentation, I would like to invite the presentation by Oved Amitay and he is speaking on behalf of all of the advocate organizations. And, we have Ben HsuBorger who is representing the ME Action, Charmian Proskauer who's representing MASS ME/CFS, and, sorry, and Ken Freedman who's representing New Jersey ME/CFS Association. So, Oved, if you could.

*Oved Amitay:* Thank you very much. Do I bring up my own slides or?

*Dr. Elizabeth Unger:* No, I think that Monica, you have the slides? That was my understanding.

*Monica Payne:* Yes, give me one second.

*Oved Amitay:* [Slide shows title page] Thank you, thank you very much. And first I would like to thank the organizers for inviting us to share the community's perspective on the needs and the barriers to care for persons with ME/CFS. My name is Oved Amitay and I serve as President of South ME. Next slide please.

[Slide shows logos from ME/CFS advocacy programs] So, I'm honored to speak today on behalf of organizations, you know, representing the ME/CFS community. Together we bring international, national, and state level perspectives that were formed over many years. I'd like to thank the many advocates who contributed to this presentation and the Massachusetts ME/CFS and the Fibromyalgia Association, ME Action New Jersey ME/CFS Association, and South ME, the organizations who worked together to put together these slides. Next slid please.

[Slide shows key talking points about ME/CFS] So, in this form I probably don't really need to describe what myalgic encephalomyelitis/chronic fatigue syndrome or ME/CFS,

as we'll refer to it, is. I'd like to only point out the complexity of this disease coupled with the lack of commonly available diagnostics and the fact that there are no approved treatments are obviously at the root of many of the barriers up here that we'll discuss today.

So, as you've already said, Dr. Koroshetz, making a diagnostics treatment and ultimately a cure become a reality really remain the key [inaudible] needs for people with ME/CFS. Next slide please.

[Slides shows description of goals and percentages of people with ME/CFS, bedbound and the impact of COVID 19] So together we start with the people living with ME/CFS who need support and access to compassionate and effective care. Suddenly I'm here today to bring the voice of a concerned community. Not only are we concerned about the current unmet needs and the barriers we'll talk about for the estimated 2 million people in the U.S. who are affected by ME/CFS, the majority of whom cannot really work or even fully live regular lives. And, I'm concerned about the barriers to care that have been in place for such a long time. But, at the same time, we're, we also feel deep anx about a near future that may possible double the number of Americans suffering with ME/CFS, with a discouraging number of people who are not recovering from COVID-19. So just imagine the impact on so many people, their families, and societal impact that, that would have. Next slide please.

[Slide shows key talking points in bullet form] So how does ME/CFS relate to Long COVID and other chronic diseases? Well, there's still obviously so much that we don't know about SARS-CoV-2 about the virus itself and COVID-19. At this point, it's evident that a subset of people who had COVID-19 go on to have symptoms that are very similar to ME/CFS. And some of them need the diagnostic criteria for ME/CFS regardless of the case definition that you may use.

So, what we don't know that these diseases are the same, we understand the people with ME/CFS and the subset of Long COVID show similar needs and face essentially the same barriers to care that we will describe, that we will talk about today. So, we know enough to understand the urgency in which we must act. We believe that the integrated approach is needed and that really the way to address it is by thinking about

both communities at the same, at the same time. So, we're therefore very encouraged to read [inaudible] announcement yesterday about the newly formed [inaudible] as it's known initiative. We totally agree that the insight that we gain from Long COVID research will also answer understanding of other diseases with similar symptoms such as ME/CFS. Likewise, prior knowledge in the ME/CFS state should inform this initiative, in fact addressing these diseases and their respective community disjointedly have the potential to have harmful consequences. Next slide please.

[Slideshows color coded breakdown of key points] So, with that said, let's focus on the experiences of the ME/CFS community. This is, this slide is just a reminder that, for people like myself who don't have the long, the longer history. It's a reminder that there's been a comprehensive report that was done back in 2013 through the FDA's initiative. It's a very, it's a very recommended read. Unfortunately, from the perspective of with ME/CFS, not much has changed since that time. Next slide please.

[Slide shows key talking points in bullet form] So as [inaudible] asked us to look at the barriers and the challenges more specifically, we wanted to have a more accurate and greater understanding of what the community's facing. So, let's look at data that was analyzed by the Massachusetts ME/CFS Association. They provide direct support to individuals that may or that do have ME/CFS and are seeking healthcare. So, part of this analysis reviewed roughly 1,000 requests from the past 5 years to identify the most problematic challenges. As you can see on the graph, on the right-hand side, the overwhelming majority of people face challenges that, at the very early stages of their journey. These have to do mostly with health, with access to healthcare providers who are either experts or knowledgeable enough about the disease and certainly who don't dismiss them with disbelief. The barriers at later stages include coordination of care, documentation of disability, and inadequate social service report. We'll explore these major categories in the following slides using direct quotes from the people who were seeking assistance. Next slide please.

[Slide shows key talking points in bullet form and a pie chart illustrating challenges by percentages] So, accessing knowledgeable providers is really the most problem and need and barrier to care. And, while we would like to see many more experts, the basic

truth is that any sufficiently knowledgeable health provider can validate the experience the person is going through, avoid harmful information that is still out there, and provide support. So, when we consider the workforce development, it's not only about experts, but really getting to the primary care physician, physicians as well. Next slide please.

[Slide shows key talking points in bullet form] The small number of experts nationally creates a very limited access to their expertise. Practically, as you can see in this quote, many people are facing long waiting periods that can be many months or even, or even a year before they can see a knowledgeable physician, let alone an ME/CFS expert. Next slide, next slide please.

[Slide shows patient quote] Disbelief is one of the most difficult aspects of ME/CFS. Many people with ME/CFS face disbelief in their own families or workplace. But a dismissing by a healthcare provider is particularly hurtful and can lead to long lasting damage. As this person says here, the only thing worse than going through this is not having anyone believe me. Next slide please.

[Slide shows patient quote] So, we'll hear later on from [inaudible] about the challenges of the medical education. And this is just so critical because it provides us with [inaudible] care about ME/CFS even without being experts, there is still a lot that they can do. On the diagnostic side, certainly even without the full, the full expertise in the disease, they could ask about the diagnosis about breaking silos and communicating with other people on the care team. They could certainly try treatments. They have, they have provided benefits for some patients, although they're not indicated for ME/CFS. Next slide please.

[Slide shows barriers for diagnosis and treatment] So, the diagnostic honesty can take years in some cases. You know that really remains a major barrier. That takes a significant toll both personally and financially. The results could be devastating as you can see here in this quote. Right now, everyone is just pushing pain meds on me and psych drugs. And that's a very, that's a very painful reality for so many people. So, reaching a diagnosis more quickly could help to avoid years of agony and wasted resources. Next slide please.

[Slide shows quote from a parent] Children and young people with ME/CFS face, and ME/CFS face particular challenges. As they often have less autonomy for sure. But parenting a child with ME/CFS brings the need to coordinate care who are working, dealing with financial burden, and of course the frustration that's caused by the disbelief as described by this parent. Everyone treats her daughter like this is psychosomatic and she cannot get any accommodations at school. This continues to be very, very painful, of course, for the children and the parents. Next slide please.

[Slide shows talking points in bullet form] So obviously, cost is a major concern for most people. The data suggests that individuals diagnosed with ME/CFS have incurred medical costs that are four times higher than those in the general population. So that gives us a context to understand what the burden of specialty care expenses, specialized tests, drugs, and supplements that are not covered by insurance might be. And, of course, it may lead, in many cases, for people to completely exhaust their financial resources. Next slide please.

[Slide shows patient quote] As I mentioned earlier, about three quarters people with ME/CFS, based on the data that we have, cannot maintain a job due to their condition. Therefore, many of the community do not have employment provided healthcare insurance and only rely on Medicaid. Unfortunately, many doctors don't accept Medicaid which leads to very few options to access care that the people need so badly. Next slide please.

[Slide shows patient quote] So, disability's a particularly sensitive topic. And while getting on Disability is not something that people would choose for themselves to begin with, even getting the correct documentation to support Disability claim prove to be a major barrier. Finding a doctor that's capable of understanding the illness and willing to help with the required documentation, as you can see in this quote, is critical. The challenge in finding physicians who are willing to do that leads to the result that most people with ME/CFS does not really apply for Disability or that they have their applications rejected. Next slide please.

[Slide shows side by side of patient account and barriers in bullet form] So, we come with many of the challenges that individuals experience, yet the challenges are not

really personal in the sense that many of them arise from structural barriers. So, I want, in the next slide, I wanted to take you through a particular story. This is Jane's story, that helps us to understand what a, what a common story is really all about. And, of course while this story's common, there really isn't any difficult ME/CFS patient. The people with ME/CFS are, they're a heterogeneous group. In this case, Jane's tried to recover after a case of mono, the Epstein-Barr virus infection. Her healthcare provider tells her to exercise and push herself. Jane gets worse. She's scared. She's bounced from doctor to doctor. Jane is told to seek counseling although mental health symptoms were only secondary to her condition. She remains sick, counseling doesn't really help, and her employees now threatened to fire her. Jane remains undiagnosed and her provider will not provide the documentation for disability. And so, the structure barriers here really include the poor medical education, the topic that we were discussing today, which is compounding by ME/CFS has no clear home in the medical specialty or otherwise, leaving people undiagnosed or misdiagnosed.

It's important to note that mental health professionals are not equipped to support people with ME/CFS. For instance, there really is no psychiatry CME for ME/CFS. There's no workplace education about managing ME/CFS. And therefore, there are no accommodations that are given without a diagnoses or doctor's orders. And, so the result is most people with ME/CFS do not apply for disability, and as I said, in many cases those applications are rejected. Next slide please.

[Slide shows patient and account and barriers in bullet form] So, Jane's story continues. She finds information online; she recognizes herself that the symptoms suggest ME/CFS. She returns to her doctors with online information, but she's told that ME/CFS is not a real disease. She tries to find an ME/CFS specialist. She gets on a waiting list, despite the cost barriers, and the providers are asked for a telemedicine consult with her current medical team. Jane remains undiagnosed now for nearly six years. And she's most likely to be singled for life.

So, I'd like to highlight one specific barriers can get, that is getting very more important now than ever before, which is access to telehealth or telemedicine. While the use of telehealth has increased significantly during COVID, we're facing coverage cuts now by

insurance and in addition from all the legal complications from telehealth across state lines and of course prescribing over state lines. This is a barrier that can be and should be addressed. The delays of these actual barriers are critical because interventions in the early stages of the disease, in the first two years specifically, improve long term health outcomes. The recovery rate in later years is much lower. And, of course, this is particularly important as we think about the implications to Long COVID. Next slide please.

So as Jane reaches the advanced stages of her disease, she is now disabled, and home bound. It is important to point out that ME/CFS is not recognized, a recognized condition for most service providers. Therefore, home care services are usually not covered. And, as we said before, there are no federally funded clinical trials nor FDA approved treatment leaving Jane with little to look for. Next slide please.

[Slide shows breakdown in percentages and other talking points in bullet form] When we consider all the challenges and barriers we discussed, it is important to recognize there are additional barriers that come with being, for instance, a person of color. Healthcare inequities create even bigger barriers. We know that children, people who are severely affected by the disease or that are in underserved communities are all facing even more extreme challenges. I also wanted to note that, although veterans are more likely to have ME/CFS, the VA website for instance still contains harmful language describing ME/CFS as a, as medically unexplained and likely to be a psychological disorder. Research suggests that the providence of ME/CFS is higher in these communities than what you may see in ME/CFS specialty clinic or frankly in the representation in our own organizations. So that is something that we all must work to address. Next slide please.

[Slide shows vision in bullet form] Thank you. So, in discussions, in discussions prior to this meeting, we were thinking about what could really be division? What would we like to see? So, painting this challenging picture, what can we do? So, our vision is to position our position structures such as this working group into agents of change. We see the need to have them place ME/CFS and local interagency structure that has resources and accountability that can guide and implement the investments and solutions that is commensurate with the seriousness of the problem. Specifically, this

would, this would address the structural challenges that we are talking about today. It would lead, plan, and execute, not just provide an advisory role. We feel that there is a need for a comprehensive five-year strategic plan specific target goals and of course to foster the interagency collaboration and coordination. Next slide please.

[Slide shows key points in bullet form] From our perspective, there's some inspiring examples that we can see of what can be achieved when a coordinated effort is applied. One such example that we wanted to highlight is the Interagency Autism Coordinating Committee. This is a federal advisory committee that coordinates all government efforts, it provides advice considering health and human services related to autism. It includes both federal and public members. And helps to ensure that a wide range of ideas and perspectives are represented and discussed in a public forum. And, perhaps, important to note that it has paid staff for support. Another example is the Ryan White Act which is also an example of what can be achieved when the right resources are created in a coordinated way, even if facing such a big challenge as HIV AIDS. Next slide please. So. Next slide please.

[Slide shows key points in bullet form] So, for the people from the various agencies in the audience today, you can ensure that ME/CFS patients are part of your agencies and part of success, really appreciate that. Together we can face this crisis. People with ME/CFS need to have full and direct participation in the policies that effect their own lives. And we feel that the interagency working group meeting, such as the one that we're having today are appear to be important for a step. But ultimately, they must lead to a coordinated comprehensive efforts and permanent community seats at the table where quality decisions are made. Next slide please.

[Slide shows key points in bullet form] So, in summary, we believe that there is a need to create a community and agency structure with the mandates to make a comprehensive plan with defined milestone and resource commitments. Designate a person that is accountable to coordinate all the HHS response, to proactively engage the community and other key stakeholders, for instance medical societies, create a clear funding recommendation to accomplish the cross-agency plan that matches the disease burden, and the scientific opportunity that we see. There's a need to create the

research and [inaudible] development through public private partnerships that are needed to expedite the progress, and, the topic of today's discussion, build capacity and improve access to clinical service for ME/CFS patients regardless of geography or income. Next slide please.

[Slide shows question and discussion topics in bullet form] So [inaudible] would like me to leave this slide for some questions for discussions. But here are some questions that we would like to propose for discussion today.

*Dr. Elizabeth Unger:* Okay. Thank you. Thank you very much. That was a really very comprehensive presentation. I appreciate the work and the thought that went into that. I think those questions. I mean, you've documented the problem and you've made some suggestions about what, how to approach it. And so I think some of those questions that you have, Monica, perhaps you could save that slide and we could use it at the end when we get to the overall discussion. Because we're still at the point of trying to flush out the problem. And, I think you have done, you've covered really a lot of the, a lot of the area. Are there other comments that people want to make about, particularly from the patient perspective. We do, we should probably get on to the Clinician Coalition presentation. It's approximately 2, so we do have some, we do have some time if anybody has any comments or questions. I really appreciate that, that the organizations all work together on this that really. Yeah, so Monica, that slide, when we get to the end of the day, we'll have discussion and suggestions and that will be helpful to help us organize our thoughts. Yeah, some of them. I think there'll be a lot of questions and suggestions, I hope, as we, as we go along. But these are excellent to keep in mind. Yes Ben.

*Ben HsuBorger:* Dr. Unger.

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* Yeah, I just, I just thought I'd often one comment and anecdote for the new members here. I mean, I assume a lot of this content is familiar to many of the members who've been working on an ME/CFS and understand the depths and the gravity of this issue. And we do, as organizations came together, you know, it is very

challenging just looking at the depths of the problem, how interrelated it is, and really what patients are facing, myself as a patient and the many people I speak with that. And I just want to remind those who may be newer to the community or newer to the discussions, you know, this Oved's presentation of the Jane story takes you to a very kind of common description. And of course, there are many [audio skips] other experiences that people are having.

And just one recent one that happened, we had a person with a severe ME at least part of it, kind of 25% severe [inaudible] group who had was losing weight, was not able to keep up their weight. And, they had to check themselves into a hospital because they did not, they were in danger of not being able to maintain their weight. They went in, they saw doctors, the doctors ran like a normal dash quote tests, MRIs and other things. They couldn't find anything wrong, quote unquote, wrong from the chemical tests and so that immediately led them to conclude that it must be a psychological issue. And so they actually implemented a psyche, a psychiatric hold on this person with severe ME who went in for basic care.

And we had, it was really, it was troubling because I've seen all of the advocacy organizations like everyone I know, and many people on this call reach out to try to contact the hospital to communicate standards and care for people with severe ME to understand these issues and to communicate to them that a psychiatric hold was totally inappropriate and actually harmed this person with ME. People with severe ME have light and sound sensitivities and psychiatric institutes; places are not equipped to deal with the complex needs of people with care.

And so, I just really want to emphasize that it effects all people with ME differently. But really, they're very, very vulnerable people who these structural things cascade upon and have damaged. So that issues is only resolved not through outreach, through a legal fight. And so that is the extent to which there are people with severe ME who are, you know, raising funds for medical and legal on the internet on GoFundMe accounts, to try to care for themselves. So just to get, offer that, when we are talking about some of those things, all of us are at risk when facing challenges, some more than others, and people's lives are on the line. And thank you, this group for coming together. These are

two very important days to see how we can move the conversation forward. So, thank you.

*Dr. Elizabeth Unger:* Yes. Thank you. It is really important that we work together and keep moving this along. So, I would now like to, I guess, shift to the clinical viewpoint and what the clinicians face. And, Dr. or Mary Dimmock has organized the Clinician Coalition. And she volunteered to do a survey of these members. And she's going to explain a little bit to us about the Clinician Coalition to get their perspective on what barriers they face in caring for patients. Because as was pointed out, many times these are systematic barriers. And we've invited Dr. Nancy Klimas from Nova Southeastern University. And she is a member of the Clinician Coalition. But we invited her specifically to comment on the challenges that academic clinicians face in establishing an ME/CFS clinic. And so, Mary if you could talk to us about the Clinician Coalition Survey.

*Mary Dimmock:* [Slide shows presentation title] Thank you Dr. Unger. First off thank you to the organization of this meeting for the opportunity to present today. My name is Mary Dimmock and I'll be presenting, as the doctor said, the results of the survey of the US ME/CFS Clinician Coalition about their experiences in providing care for people with ME/CFS and also in engaging the medical community in that care. The views reported in this survey will also echo what we just heard from Oved.

I partnered with Cindy Bateman starting in 2018 to organize the Clinician Coalition. The coalition has 21 members who have collective spent hundreds of years treating many thousands of patients with ME/CFS. There are a mix of internists and a few other subspecialties. Less than half have clinics in academic centers. Their clinics are in independent practices. Three are already retired, and a number are approaching retirement age. That's an important fact to keep in mind as you think about what needs to be done to address the clinical care for ME/CFS. The Clinician Coalition's goals are to document the best practices, to educate the medical community, and to provide clinical insight to research.

*Dr. Elizabeth Unger:* Excuse me.

*Mary Dimmock:* Sorry?

*Dr. Elizabeth Unger*: Excuse me Mary. Are you remember to tell them to advance the slides? Because.

*Mary Dimmock:* Yes, I am.

*Dr. Elizabeth Unger:* Okay.

*Mary Dimmock:* I'm just going to give them some background here. All right. To advance the clinical care goals, the Coalition has developed consensus statements and recommendations, deployed a website for medical providers, and prepared a manuscript for publication on diagnosis and management. Coalition members are also involved in research as clinical partners of many of the research being done here and have also undertaken a number of the educational efforts that will be discussed later. Next slide please.

[Slide shows patient population breakdown with cost and percentages] Not surprisingly the survey results underscore what we already know. We have a problem with access to clinical care for people with ME/CFS. That can't be fixed without your leadership and that of key medical associations and institutions. Next slide please.

As highlighted earlier, there are an estimated 1 to 2.5 million Americans with ME/CFS with whom an estimated 75% can't work and 25% are home bound or bed bound. And, as you all know, this is a chronic disease that can last a lifetime. And now, as the result of COVID, as Oved said, the prevalence of ME/CFS could grow dramatically. At a recent publication, doctors Anthony Komaroff and Lucinda Bateman know that the numbers of ME/CFS patients could double in just over a year as a result of the pandemic. Next slide please. Next Slide.

[Slide shows map of U.S. stars represent clinic locations and patient breakdown in percentages] Thank you. For that one, I'm sorry, back one slide. For that 1 to 2.5 million people, there are an estimated 15 or less ME/CFS clinics and less than 20 clinicians in active ME/CFS focused clinical practices across the country. This includes just one clinic for pediatrics. The survey didn't ask about patient demographics. But we know

from a publication of CDC multi-site study seven of these clinics that the patient's see are overwhelmingly white even though ME/CFS effects all races. The survey also didn't ask how many patients each clinician sees. But one clinician reported 1,000 active patients and another reported 2,000. If that represents what the others are seeing, it's still a very small percentage of the total ME/CFS patient population.

Finally, it's important to note that 25% who are home bound, that 25% of patients who are home bound, or bed bound are probably not getting to see these clinics because they can't travel. And they are likely also struggling to get local care as well. Next slide please.

[Slide shows color coded table with talking points in bullet form] Now to the survey itself, 14 of 21 coalition members responded to the following questions. Are their patients self-referred or clinician referred? Do the clinics accept insurance? And, if not, why not? What challenges are experienced in engaging other clinicians in the care of their patients or in attracting other clinicians to join their practices? And what are the barriers to increasing the number of knowledgeable willing clinicians? What have these clinicians done to educate the medical community and what impact has that had? And, finally, what needs to be done to increase the number of willing knowledgeable providers to address the access issue that was so clearly called out in the chart that Oved presented? I'll go through each of these responses to the questions next. Next slide please.

[Slide shows pie chart of referral sources and percentages] Starting with referral, 50% of the clinicians said that the patients were self-referred, 20% said that the patients were clinician referred, and 30% said that there was a combination of the two. The survey did not ask why this might be. But some of the responses to later questions might suggest that the lack of recognition of ME/CFS and these clinics by the medical community would play a role in that. Next slide please. Thank you.

[Slide show color coded challenges in boxes and key points with percentages in bullet form] The next questions were on insurance reimbursement. As we, as was pointed out earlier ME/CFS is a complex disease that requires significant time to diagnose and manage. Clinicians reported taking two and sometimes as long as three hours for initial

appointment and follow up appointments can also be long. They also spent additional time revealing medical records, which can be expensive, supporting Disability requests, which is, as noted earlier, can be challenging, filing insurance appeals to get coverage, and addressing support needs which, especially for the severely ill, can be significant.

The amount of time clinicians spend on visits and these other activities is not reimbursed by insurance. A few doctors note with the lower reimbursement rate, this is especially problematic for the internists in the group. As a result, 50% of the respondents said they do not accept insurance, 21% said they only accept Medicare or Medicare plus one other insurance, 21% do accept insurance, and 8% accept insurance but also use a [inaudible] model on a sliding scale to help offset the lack of reimbursement from insurance. Lack of, lack of reimbursement and reimbursement issues doesn't just effect clinician time, it also effects their ability to provide the necessary office procedures, tests, and treatments.

Some clinicians said they can get tests covered, but much more commonly, they reported challenges with getting coverage for both tests and treatment and even in some cases for basic or common ones such as those for orthostatic intolerance often seen in ME/CFS. One clinician noted that the insurance may require the first prescribed series of other treatments before being finally allowed to provide the treatment they knew was needed to begin with. Another clinician noted that the treatments are used off label because of the lack of published evidence and research. And that, that makes it easy for insurance companies to deny coverage. They also said this can affect dated tests.

One clinician described the result a daily nightmare of preauthorization's and peer to peer reviews and finally appeals that can take hours and hours and extend over weeks to months. One clinician noted that the appeals are typically successful, but to get there he had invested a significant amount of time and that the patient had been left waiting for months. While it doesn't fix the problem, clinicians have reported that it can help improve coverage by documenting coding and a comorbidity such as POTS Mast Cell Activation Syndrome etcetera because these may have better coverage than what

ME/CFS does. Now, it's, some of these issues effect other people within the clinical, other clinicians outside of ME/CFS. They're not unusual.

But I would say the magnitude of the issues are particularly severe with ME/CFS because of the reasons mentioned here and also discussed further below. And, a lack, this lack of, as a result, this lack of reimbursement will impede ME/CFS clinical care by any provider, not just these experts. Can you go to the next slide please?

[Slide shows color coded challenges in boxes and key points with percentages in bullet form] Excuse me. The next questions were about the challenges these clinicians experience in engaging the medical community, either in the care of their patients or to come work at their clinics. Patients may not always have a PCP, but when they do, a few respondents said these PCPs can be quite engaged. But, more commonly, respondents reported that PCPs will rarely engage. Excuse me just a minute. A variety of reasons for those were noted including, as was noted by Oved in his presentation, the PCPs can be dismissive, don't believe the disease, or think it's psychosomatic. They don't understand ME/CFS or its treatment and had no exposure in medical school to the disease. They feel it is too complex and too difficult to manage. And, really importantly they’re, and we'll come back to this, they're uncomfortable practicing outside of the evidence base and standard medical practice and they're put off by the lack of diagnostics and FDA approved treatments.

Finally, they don't have the time in their practices and or they could be penalized by their health plans for spending too much time with patients or thinking outside the box. Some clinicians have said that it's easier to engage specialists than PCPs, but others felt it was just as difficult. A few did note that the situation with the pandemic may be starting to improve, sadly, may be starting to improve the situation because more attention is being brought forth. The survey also asked about additional challenges with getting clinicians to join their ME/CFS practices noted before the number of clinicians is very small and a number of them are approaching retirement. And we really need to expand the number of clinicians in the field. But the additional challenges that they noted was the view that the practice is, could be considered too narrow and too off track for a normal clinician career. The ME/CFS in the slide says the patients, but this should

really ME/CFS is too complex and demanding to manage and that it's difficult to provide a competitive salary with a new clinician to the practice without increasing rates. Next slide please.

[Slide shows color coded challenges in boxes and key points with percentages in bullet form] The next survey asked about the barriers that would need to be addressed to, in order to increase the number of PCPs and specialists willing and able treat patients, people with ME/CFS. It also asked about the barriers to increasing the number of ME/CFS since the pool of experts is small. These questions, these answers are going to overlap somewhat with what was done, was said previously. The responses for increasing the number of people, physicians willing to treat and increasing the number of experts overlapped and so they're grouped into four themes. The top five responses are bolded. The first theme involves the stigma towards ME/CFS, the lack of knowledge about the disease and how to treat it, and its perceived complexity as was discussed earlier. Respondents added that many clinicians perceive there is little they can do to help with ME/CFS and or they did not want to manage chronic illnesses.

The second theme also previously discussed is the lack of reimbursements that have come up a number of times throughout this presentation. And, for both the clinician time and for the test, treatments, and support services required to care for these patients.

The third theme is the lack of research, especially the lack of formal clinical trials, evidence for treatments. This is critical to address the workforce planning when you consider that the respondents' comments for clinicians being uncomfortable practicing outside the evidence base and being put off by the lack of diagnostics and FDA improved treatments. This lack of evidence makes it difficult to engage them in the care of ME/CFS patients. In addition to the lack of research, some respondents also noted that the slow pace of research can also impact the perception of the field.

And the fourth theme is the lack of support from medical institutions and peers from clinicians caring for people with ME/CFS and the lack of support services to help people. Some of this is direct, you know, peer to peer, doctor to doctor, you know, whether the other doctor that you're trying to work with actually respects the work that

you do. This challenge, this issue is also challenging for those who are home bound, bed bound, and especially for those needing total care. Next slide please.

[Slide shows color coded challenges in boxes and key points with percentages in bullet form] The next question asked about the approaches these clinicians have used to educate the medical community. And they've taken a variety and do take a variety of different approaches across the board. A number of the respondents report providing onsite learning opportunities such as rotations for premedical students, medical students and practicing physicians. One respondent, whose clinic is in an academic center, reported providing up to 24 rotations a year for first through fourth year students across both their clinic and their research program. But, more typically, respondents reported providing a few rotations per year at most. Sometimes they were for premed students but more usually for practicing physicians who would visit for a brief period of time, a couple of days I think was the most common answer. One respondent noted that those going through the rotations typically did not go on to focus in ME/CFS, but at least they were more aware. All these rotations were seen as valuable. A few respondents noted that many physicians were not interested in or can't take the time away from their own practices. And another respondent said that providing these rotations slows efficiency in an already financially strapped system at their clinic.

A number of respondents called out the need for funding to support these kinds of more intensive learning opportunities if we want to move forward. The clinicians also said that they provide a variety of informational material for providers such as primaries, handouts, articles, links and websites, especially websites and online education material that they've produced at their own clinics. But some said that physicians aren't interested in and they suspect the materials are much more often used by patients than by providers.

Finally, the respondents said that they have also done CMEs presented at conferences, provided tele mentoring, and medical consults on specific cases all of which helped increase the knowledge of their clinicians. One respondent noted that list serves have been particularly helpful because it provides a case-based form for discussing and learning about particular cases. The clinicians have also offered documents for

publications in the medical literature. But it's worth noting that getting an ME article published could be its own challenge, particularly given the lack of research, supporting published information, and even the misperception about the disease. All these methods have their place and are seen as being effective at least when the clinicians are interested. But, even if all the clinicians were interested, this is just a handful of doctors. And we're only talking, we're only talking about a small handful of doctors, and they can barely touch the magnitude, the need that we have. Next slide please.

[Slide shows color coded challenges in boxes and key points with percentages in bullet form] The final survey question asked what needs to be done to increase the number of doctors willing and able to care for people with ME/CFS? First respondent, first the respondents noted the need to repute the significant information about the nature of treatment of ME/CFS and to provide a range of educational opportunities to build basic knowledge and provide the kind of advanced learning gained through telemonitoring and onsite rotations. Excuse me. One clinician noted that refuting the information must address the participant belief that the disease is psychosomatic and can be treated by cognitive behavioral therapy. Addressing this kind of, refuting the misinformation and also providing the learning opportunities that are named is going to require a comprehensive plan and substantial funding including specific funding to support those richer online, those richer learning opportunities such as rotations and telemonitoring. It's also going to require strong leadership and commitment from federal agencies and importantly medical associations. One respondent noted that while there are clinical guides, many clinical guides for ME/CFS, none have been accepted by the American, I'm sorry, American College of Physicians. That's probably true for other key medical associations as well. How far will any educational program get if these associations are not involved?

Second, reimbursement, reimbursement, we've talked about it many of times. That system needs to be fixed. It needs to reimburse care based on the time and complexity of ME/CFS and to cover medically appropriate test medications and support services. This includes the addressing the issues with telehealth insurance, with cross site healthcare and also support services that Oved mentioned earlier. Federal agencies,

insurance companies, and healthcare health provider plans will need to be involved to make this happen.

Third, and related, is getting the health institutes, the academic centers, and the health plans to provide incentives, not punishment for those providing care for, I'm sorry, chronic complex diseases. One respondent noted a gastroenterologist was so pressured by her academic center to see fewer complex patients and do more procedures that she left medicine and went into research. Such incentives much also cover care for the severely ill.

Fourth is the need for diagnostics and for FDA approved treatments or at least published evidence for treatments already being used off label. This group of clinicians has called for clinical trials for a number of the medications they're already using off label. Research and research funding must become a more substantial priority. And finally, a team-based approach is required to provide the care needed for ME/CFS patients. In addition to PCPs, this must include the key subspecialties plus physical therapists also occupational therapists, case managers, support services, etcetera. This could be achieved through the clinical care centers who locate these disciplines and provide ongoing care, over the course of the patient's illness, not just for six months. But, at the very least, this will require outreach and active participation to these critical disciplines. Next slide please.

[Slide shows key talking points in bold colors] It's impossible to overestimate the significant issues that exist in positioning clinical care for people with ME/CFS. This obviously has had a significant impact on patients throughout the country and will impact any Long COVID patients who go on to develop ME/CFS. But it's also important to note that it's had a significant impact on the clinicians who are trying to provide care for these patients. One clinician noted that the current situation with ME/CFS is creating burnout in the very limited supply of these clinicians. And he noted that the flood of post COVID patients will and is already making that situation magnitudes worse. There's a likelihood that the pandemic could significantly increase the number of ME/CFS patients and that the pool of ME/CFS clinicians is small and often older. This is an urgent crisis that must be addressed quickly. We need your leadership out of key medical societies,

medical institutions, academic centers, and health plan specifics. Thank you very much. Thank you, Beth, Dr. Unger.

*Dr. Elizabeth Unger:* Thank you Mary. And thank you for your leadership. And you were very key in organizing the Clinician Coalition which I think has been a very effective group for advancing this field. And I think the comments about so few of the ME/CFS clinicians being academically based is very important. Because it's the academics that really lead the research. And academics need to understand the illness in order to make the advances that are necessary. And that's why I thought it was important to take a moment to really, specifically comment on barriers that academic, academic clinicians face in having an ME/CFS. So, Nancy, if you could take a few minutes to comment on that. And, then we'll have a bigger discussion.

*Dr. Nancy Klimas:* Yes and thank you. And Mary that was really a very nice discussion from the clinician's perspective about what we're seeing. I want to tell folks who don't know, who don't remember this or don't know this. There was a paper by Lenny Jason some years ago that said, basically, that clinicians that were most likely to know what to do or at least recognize the illness when it walked through the door were the clinicians that had the illness in their families. Not only we failed to teach them, we weren't teaching it at medical school, we weren't' teaching it in residency, we're not teaching it in post residency CMEs. And, at that time, and it's not changed very much since, only 15% of the ME/CFS cases in the country had received the diagnosis. Meaning that 85% of the time, if you walked through doctor's door, the doctor wasn't knowledgeable enough to recognize the illness and at least to diagnose if not treat it.

So, I think we're in that situation still today. It's not very different. But we put this pandemic overlay on top of what was a weak system to begin with. The HHS has an advisory committee for ME/CFS or had for many, many years. And many, many years, year after year, one of the number one recommendation was to create centers of excellence, clinical and research centers of excellence so that there could be epicenters of educational as well as research in clinical care, much as we did with the cancer centers earlier in that space and that type of thing.

So, and that hasn't been the past yet. So let me tell you about our academic, our experience. We're an ME/CFS clinic, focus clinic at Nova Southeastern University. We're the Institute for Neuro-Immune Medicine. And we assembled about 18 faculty members and another 40 or so lab techs and other support people to do a combination of research and clinical care in a space that was trying to do the three pillars, communication, research, and care. The three pillars that we, that need to be done. I know we; we're pleased that we've managed to assemble and do much of that. But, before COVID happened, if you backtracked one year ago, we had 400 patients on our wait list, and it was taking two to three years to get an appointment in our expert clinic. That's shocking. We have now 6 practitioners that's probably one of the bigger clinics in the country that's focusing on this. And so, we're kind of, you know, 6 is not nearly enough to take off, I think we've got 3,500 patients in our, in our care.

So that's where we were before COVID. Recognizing, in our research experience, that there's a narrow window to intervene before something that is just a lingering chronic illness turns into a lifelong miserable illness. And that, that window's probably right now for the post COVID people, an intervention should be happening now and not after we've studied it for four or five years. We have to think about things a little differently right now and be very responsive to the needs of the patient population even in the absence of evidence-based guidelines. We know a lot about ME/CFS and we know a lot about this care, partly from the seat of our pants, the Coalition, the Clinician Coalition has shares a lot of common experience and knowledge in part through what little evidence-based mechanisms in clinical trials there have been.

And I will emphasize the word little. Because I studied another illness called Gulf War Illness where the funding mechanisms for clinical trials are aggressively put forward particularly in the CDRMP program where advocates are extremely involved in the priorities year by year. And the calls for proposals every single year change in response to new knowledge of the prior year. And we don't really do that in our other funding agencies very much. But I will say the CDRMP, if you looked at Gulf War Illness, you'd find 23 active clinical trials. And you wouldn't find that in the other spaces where funding might not be happening, not that the trials are not happening, but not 23 I mean, it

hasn't happened. And the CDRMP funded a clinical trials network grant to fast forward, translate [inaudible] stuff out there. So as clinician who's also an investigator, I'm going to say I feel a little tired. Because we are supposed to be doing evidence-based medicine as much as we can, even in ME/CFS, despite 30 years of my career, 35 years of work where, certainly, we understand the underlying underpinnings and even have targetable points, we haven't had the kind of funding needed, the evidence base, the guidelines that would allow us to do that kind of work enter a pandemic and post COVID Care. And so this is what we're doing.

Is what, could you, yeah, I think there's lots of needs and we, we're going to be talking about the COVID, particularly the Long COVID and the relationship a little bit more tomorrow. But for today, what were the unique challenges? I mean why aren't there more academic clinicians?

The [inaudible] challenge on our side, which is probably one of the better sides that should be able to be responsive to something, we have, you know the expertise. We had to make the hard decision whether the 400 people on that wait list who have been waiting for years, needed to wait longer so that we could get these post COVID people in as fast as we could and hope to intervene early in their course, think ethical department. And you can't believe how much time we spent discussing that in our group. Nonetheless, we're trying to find ways to get people in. And we realize it's completely inadequate.

So, this is what we're doing to try to reframe. We're creating our post COVID Care Clinic at our university. We're going to do a much better job with smoking mirrors and no funding, we just hope to be able to do this. But, to take our clinical group, that is the ME/CFS expert group and use it as a tiered approach.

So, we're going to use the primary care network that is at our university, internal medicine, family medicine, and then there's practitioner and primary care clinics that are across the state, and we're going to be their backbone. We're going to teach them what to do. We're going to give case management conferences every week, bring cases in, and support the primary care network in being better at this. For this we think they're finally pushing out knowledge that is useful to the primary care providers who want to, I

mean don't think that most doctors want to push you out of your office. They don't know what to do when they see you. And that feels bad when you're a doctor and you're looking at something going oh man this person's sick. But what do I do? And, then not have any place to refer them to that makes any sense. So instead, we're going to try to give them the tools they need to do the initial evaluations to do that kind of thing. But back them up with the expertise of our group. So that's our plan. It would work a whole lot better if there was a funding mechanism. Because, you know, basically there's no new people or money to do anything with. So, we're trying to ask people to make space in their clinics, their already busy clinics for more patients and for us to make space and time in our practices.

Right. Be more supportive. But that's what we're going to do and then we're going to pursue money and we hope to someday find some support to push this out.

So, trying to reframe, in general, from an academic clinician point of view, did you have trouble getting your administration to allow you the extra time that was needed? I mean is it a structural barrier like that or is it a lack of understanding of the, of your department's you know whatever department you're in, internal medicine or infectious disease of the illness? I mean I'm just trying to understand why there aren't more academic physicians caring.

That is my only problem, the one that I left the university for. Well. That, got it. Yeah, so.

So, I'm in osteopathic medical school. I left an allopathic school where I was not functioning well. I wasn't providing the needs of the patients. And, I went to an osteopathic medical school, Nova Southeastern which has been very welcoming and gets this total body integrative complex medicine. It fits into the way they teach. So, I've been very happy being an MD in a DO school. I don't fit personally but my field works better. And we housed a whole practice in the integrative medicine, functional medicine space which works great for ME/CFS. That's the place to house this, which is not to try to force fit a square peg in a round whole all the time. This works really well in an integrative medicine space.

And, then using specialty care as needed if you need ID or whatever to twist this thing, you can do that. So that is one thing is trying to find the home institution that wanted us. And we did, we found that. And it's been a very supportive and nurturing environment for us. The other was to understand that to make the advances in research that the field needs, we had to wrap our research program around the clinical care program. And that is lacking everywhere. If you want to ask why we don't have trials? Well, who's going to do the trials. The clinical care program in an academic center can service the translational medicine unit, the thing that moves things from phase one and phase two and out into the bigger, bigger things. And so having clinics that are, that are affiliated with or actually wrapped around and are a part of a broader research program, that's a really good strategy. And, that's the strategy we have used.

So,for post COVID Care. We need patients to do the research. You understand that we need to have the capacity to see these patients.

Right. So that we can be effective investigators. And I'm telling you that we were full up to above are years, before the epidemic.

*Dr. Elizabeth Unger:* Right.

*Dr. Nancy Klimas:* So now we're trying to find the space. And we want to be expert. You know, we need clinical experience, I just had two post COVID patients this morning.

*Dr. Elizabeth Unger:* Yes.

*Dr. Nancy Klimas:* But the, but you know, you need the smoking mirrors. You just got to make it happen with nothing.

*Dr. Elizabeth Unger:* Okay. We have a hand, Dr. Katherine Argue from Department of Defense, you wanted to make a comment.

*Dr. Katherine Argue:* I just wanted to quickly response because Dr. Klimas brought up the funding that we have at CDRMP for Gulf War Illness. And I just want to make sure that everyone in the audience is aware that we do now have funding specifically for ME/CFS. It is not its own program; it falls under the umbrella program of the peer reviewed medical research program. But we specially have ME/CFS as a topic area

under that program which allows us to do funding for this very similar to what we had done for Gulf War Illness where we can fund clinical trials, large coalition type research, etcetera. So, if we need to do a better job of making sure that clinicians and researchers are aware of that funding opportunity, please let me know.

*Dr. Nancy Klimas:* Thank you. That was super helpful. Because I think what I like about the CDRMP is the role of the advocate in helping set the priorities of the program year by year, every single year, there's new, the ability to shift the focus or move things that need to go from bench to clinic forward. And, that's been really rewarding. And, it has made a big difference in a very similar illness.

*Dr. Elizabeth Unger:* And, Mary Dimmock, you have your hand, another comment?

*Dr. Nancy Klimas:* Mary you're muted.

*Mary Dimmock:* Just adding to the questions that you're asking Beth. One of the things that was brought up at the FDA meeting 2012 for ME/CFS was by the industry rep from Eli Lily. And she noted that it's really impossible for Pharma to virtually get involved if we don't have academic centers who are actually studying, treating and studying this disease. And, then additionally, from what I understand of the DOD and Nancy your work, they've set up some work to be able to build the clinical trial's infrastructure that would be needed to be able to advance these clinical trials. And we don't really have that in ME/CFS yet. And, then finally, because of the lack of clinicians at all, never mind the academic institutes, it would be hard to do the level of research that we, clinical trials research that we need to advance the disease. So, there's a set of overlapping interrelated issues here.

*Dr. Elizabeth Unger:* Yes.

*Mary Dimmock:* That need to be addressed.

*Dr. Elizabeth Unger:* Yeah. I really feel that the shortage of academic clinicians is just really key. And that's why I really wanted focus on what are the barriers. If the academic clinicians are there, they'll be part of the medical school, students will rotate through clinics, and we will solve a lot of our problems. So, I think we need to increase the

academic representation in this field. And, it is, as Nancy points out, and we're going to talk about at more length tomorrow, the Long COVID may this opportunity to really spark a true academic interest and collaboration. Ben, you have a comment?

*Ben HsuBorger:* Yes. Can you hear me?

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* Okay. Thank you, Dr. Unger. And I just wanted to add on to what she said. I think academic centers and clinicians are really important. And it would be really great to see, you know, that flow of medical students through. I do want to also make the point that, you know, for my people, what we're experiencing right now. And so, it is also really important how are we going to train, provide mechanisms that will provide the doctors that are doing it now? And the point that Mary made earlier about we have a knowledge base of doctors who are practicing right now who are nearing retirement. And that will be shrinking. And so there is both investing for the future and what mechanisms can we put in place for training doctors right now who are practicing?

*Dr. Elizabeth Unger:* Yes. As we, CDC had a study with seven different clinics, and two of those clinics have closed due to retirement already and a third is threatening. So, we have a, we're very, very aware of the aging out phenomenon and we really need to keep, to build the expertise. I got a message from people watching the question and answer. Christine, did you have some questions you wanted to share?

*Christine Pearson:* Yes. Hi everyone, I'm Christine Pearson. I manage communications for the part of CDC that the ME/CFS program falls under. So we've gotten quite a number of questions. What we decided, since we're running a little ahead right now, we'll take some of them now and then we'll save the rest for the end of the day. I did want to mention that they're, we've gotten some that are on Long COVID. And, since those are, that's going to be our main topic for tomorrow, we're taking those down and we will save those for tomorrow to intersperse with the conversation about Long COVID then.

So, the first one that we have, and this is a little long, and it's from Lily Chu. And, it says feels like primary care medicine, child psychiatry and geriatric medicine also have

workforce shortages. Many of these issues discussed today are similar to those faced by these fields. Primary among them is reimbursement. Cognitively oriented fields are paid less per minute per visit than procedurally oriented fields like surgery. Has anyone contacted the players in these fields about their initiatives? Also, how much of a role can CDC really play in terms of increasing the workforce? Unlike other countries, we don't have a national healthcare system that addresses appropriate workforce balance.

*Dr. Elizabeth Unger:* Well thank you, that's.

*Dr. Nancy Klimas:* Can I make a comment on that? There's one thing that federal agencies can do which is get ME/CFS and this post COVID on this, on the list of complex illnesses that are reimbursed at a higher rate by Medicare. Because Medicare sets the standard. And that allows you to spend more time per patient. Right now, things like diabetes and congestive heart failure are on the list. But you have to be on the list to get that extra reimbursement. And it gives you a chance to be spend more time per patient. So that is one.

*Dr. Elizabeth Unger:* Okay.

*Dr. Nancy Klimas:* And Lily, I don't think we're going to solve the problems of not enough doctors. But we want to entice some over. And in academic medicine, research funding is very enticing if it can go to physician scientists as well as to bench scientists. This idea that there's clinical science opportunities and it's not restricted entirely to bench science. And I would make a huge plight for a clinical trials network. And the other thing has let us not forget that ME/CFS and post COVID illness are compared in their illnesses and it's straightforward to include ME/CFS in the grants that we write as the comparative on this. And so new work can be done on the back of the new post COVID monies that will be coming into the research field.

*Dr. Howard Selinger:* This is, this is Dr. Selinger. Can you all hear me?

*Dr. Nancy Klimas:* Yes.

*Dr. Howard Selinger:* I want to make sure you all know that as of 1/1/2021, just eight weeks ago, CMMS launched the biggest change to reimbursement in primary care

evaluation and [inaudible] since 1997. They have streamlined the documentation process. No longer does one have to worry about documenting elements of history, past family medical, social, and physical exam. They have increased the reimbursement for time based. They have allowed time-based codes to include face to face, non-face to face, and the review of records. And they've also increased the medical decision-making reimbursement. Again, the biggest change and although doctors are aware of it, they need to link this to the awareness to patients such as ME/CFS who take more time, they can now bill and there are modifiers where you can keep adding on, adding on, adding on, time-based billing that is expected to make a significant difference in the reimbursement for primary care.

*Dr. Elizabeth Unger:* Well thank you for pointing that out. Did you say that was CMS that made the change? And if so.

*Dr. Howard Selinger:* That is C, that is CMMS and it applies.

*Dr. Elizabeth Unger:* CMMS.

*Dr. Howard Selinger:* Right. It is.

*Dr. Shari Ling:* This is Shari Ling.

*Dr. Elizabeth Unger:* Yes.

*Dr. Shari Ling:* And Dr. Howard is correct. It is Centers for Medicare and Medicaid Services. But we go by CMS and dropped one of the M's. I do not know why. But I think that was well said. I think, you know, there's been a lot of work that has been done really to better support the care that is needed that's delivered to Medicare and Medicaid beneficiaries. I will also say that I think what you are referring to is some of the complex billing codes, the modifiers if you will. Now those are, I would venture to guess that they would be applicable here, such as the chronic care management code.

*Dr. Howard Selinger:* Yes.

*Dr. Shari Ling:* And, by definition, it is operationally defined as to apply to people whose care is more complex. And, complex is defined as greater than one condition.

*Dr. Howard Selinger:* Right.

*Dr. Shari Ling:* So it is really intended to try to really provide the opportunity to provide the care that is needed. I will also say that, and I understand that this is a double-edged sword. But some of the other behavioral health codes are also applicable. Now we have operationalized that in very general terms as well. So behavioral health does not mean substance abuse disorder or, you know, by definition. But it also includes, and we have to figure out how to define this as broad, as broadly as we could to catch as many people as could be applied to. But, you know, it can also apply to people with sleep disorders and other types of symptoms that are hard to characterize.

*Dr. Howard Selinger:* Yep.

*Dr. Shari Ling:* So, I just didn't want anyone to, you know, take that code the way it's not intended to put a label on someone. But these are different ways to enhance the amount of time, acknowledge how much time it takes to provide the care that is necessary. And, you know, recognizing that.

*Dr. Howard Selinger:* Right.

*Dr. Shari Ling:* Kind of conditions that go in and out of a variety of settings, there are also care transitions billing codes. And there is to try to acknowledge that your medications may change, right, from one setting to another. And each time you have to reconcile what is needed. Some will no longer be needed, others new will be needed. But it all requires time and attention. So perhaps I can ask my team to provide a link to some of these resources that kind of summarize these different, so I don't know if that'll be helpful but glad to do. Over thank you.

*Dr. Elizabeth Unger:* Yes. Thank you, that's very helpful. I think that would be helpful.

*Dr. Howard Selinger:* And, then this needs to be rolled out to physicians on the front line so they understand how these opportunities that are new, or preexisting, can be applied to patients with complex chronic conditions like ME/CFS.

*Dr. Elizabeth Unger:* Thank you for raising that. That's very good.

*Christine Pearson:* So, I think we have time for a couple more questions before we get to the end of what was supposed to be this section. So, the next one comes from, I'm going to probably butcher this, I'm sorry in advance, Katy Debalik who says. How many institutions and clinics are doing clinical trials already? Should we begin by encouraging clinicians to consider clinical trial training as well? Multicentered trials would also be useful for all of us around the world.

*Dr. Elizabeth Unger:* Yes. We're going to talk about these issues a little bit more. And, we have a special, Dr. Vicky Whittemore is going to talk about NIH's initiative to try to increase clinical trials. If you go to clinicaltrials.gov, there are some clinical trials listed for ME/CFS. They're at this point, some of them are enrolling and some of them aren't. Then they're usually fairly small. But yest, clinical trials are desperately needed. And, I see Charmian, you have a comment.

*Charmian Proskauer:* I want to go back to an earlier topic. I'm sorry to change the subject. I think this is an important revelation actually. But I wanted to go back to the, as long as we're still on the patient voice.

*Dr. Elizabeth Unger:* Yes.

*Charmian Proskauer:* To talk to the point of how we can get the healthcare providers on the ground. The vast majority of them are better positioned to help ME/CFS patients. And I don't think this is necessarily complicated clinical and medical education. I think the point that Oved made in the presentation that just believing the patient and supporting the patient and making addressing with some commonsense suggestions about how to address the most troublesome symptoms can be helpful. But, in terms of believing the patient, there's still an enormous stigma attached to medically unexplained symptoms, I'm going to call it, which would also describe ME/CFS.

And what I think is really needed is a very, very strong statement coming down from the top that's going to reach the broad base of providers that ME/CFS is a real illness, a real serious illness and needs to be taken seriously. And, that there are some things that every healthcare provider can do.

And, to go along with that, I think there needs to be more, there need to be more articles in the broad variety of journals that cover the, the journals that clinicians typically read. And, in this area, one of those is the New England Journal of Medicine, which has not published any article on ME/CFS since 1959 or something like that. And I know there may be many reasons for that. But I think that's something that everyone needs to think about, getting, getting articles in the journals that clinicians tend to read.

*Dr. Elizabeth Unger:* Yes. Thank you. We are at, after our break we are going to talk about the things that have been tried and we will then have a bigger discussion. But these are very important points, trying to be sure that there is a consistent message about the nature of this illness. And I agree with you that primary care physicians are important in caring for these patients. And they can at least do the basics. And it does start with listening and believing. And.

*Christine Pearson:* So, to that point Beth, actually there was, there was one question which I know we've answered in other forms before. But, just in case there are people on who've not been on our other calls. This one comes from Ellen Gurwit and it says until the Federal Health Agencies declare that ME/CFS is a real medical illness, there will be no progress. All the problems you've mentioned will continue as the general population medical communities have no conviction of the reality of ME/CFS. Why has this public declaration not been made in spite of the contributions of individuals in some agencies?

*Dr. Elizabeth Unger:* Well, I will start by saying I think CDC has been very clear in making the statement that ME/CFS is an important illness and is biologically based and is not associated with malingering and needs to be taken very seriously. And, I believe, NIH has done that as well. And I'm not sure how else to make the message clearer. And we are also aware that patients with ME/CFS face stigma and we are, we do have the sense that even researchers and clinicians treating ME/CFS face stigma, lack of understanding. Somebody mentioned just today that it was harder, hard to get articles published about ME/CFS. And, that is, that does face, sometimes the reviewers don't understand or don't listen to other professionals either. So, when we come to our discussion time and plans, when, if there are concrete ideas about how this could be

done more systematically or more directly, and I don't know if others of the government want to comment on what they've done or what their thoughts are.

*Christine Pearson:* All right. So I think let's just, there's a few more that I think might have short answers maybe, so.

*Ben HsuBorger:* Christine?

*Christine Pearson:* Yes.

*Ben HsuBorger:* I apologize. Before we go on, there is one thing I'd like to know and maybe this comes back we deal with this at another point. In terms of, you know, addressing issues, I think there's also, there's a difference between, you know, a statement somewhere the CDC has updated their website in some ways and so those changes have been reflected.

But, in terms of also like, you know, when we think about people like the severe people with ME who are, you know, in front of hospital staff who are already misbelieving them, like some clear high-level communications that are put out would go a long way to like stopping immediate harm. So, I think we need to think about like higher level communications that are clearer.

I think, and two other points I'll just quickly make is, you know, to what extent that we do have, when we have pockets of knowledge in places, like how can we amplify and look that up, so there is a lot of good information coming out of, I would say, the ME/CFS Clinician Coalition, how can we get that publicized too more? How can our federal agency partners come together and get that information that's over with these experts out to the entire community?

And, then one third aspect that I'll mention that I think is important as part of this agency group, is how do we get each of these agencies delivering a clear and consistent message? So, for example, you know, look over on the, I was looking at a VA page the other day that lists ME/CFS under war related illness, about ME/CFS. And right there on the front it says treatments, some treatments for ME/CFS include graded exercise therapies, psychological therapies, and medication.

So, these are like, these are clearly not what, you know, graded exercise therapy, psychological therapies are not the recommended therapies for ME/CFS. And so how can we make sure that across agencies like a consistent message about this disease is communicated? And we deal with uneven messaging and communication. And so, I think we do need to think about like communication strategies and how we can both amplify. Thanks.

*Christine Pearson:* Sure, and let me jump in then real quick on your, the first part of your response. I do agree that you're right. Actually, one of the things that we're working on now and we hope to have them posted soon are some provider handouts. And they're very, yeah, they're written in a way that it's a general overview of what is ME/CFS even and what do people need to know? With the idea, and then we'll be working on trying to get awareness out that those are available. Because hopefully that will help with some of the sort of general clinician populations. And.

*Ben HsuBorger:* I would.

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* I would like to just, sorry. Just to make one other comment. Is that, in terms of communication. So, I know we deal with this problem of like the evidence base, from which communicate we want to be clear on our evidence base, but, and all the statements made. But to also think about when these communications go out, like, we are dealing with the medical providers often times that it's going to are people who already have stigmatized views of the disease.

So, it's also, you know, convincing somebody. And, I've been in a situation where, you know, people are committed to psychiatric units, I've been calling on the phone trying to convince them, the nurses, that they can't force this person to get up to go to the phone or get up to eat. They need to bring food to the person and not present them as malingering.

So, I think, you know, there is, there's a perspective, there may be a perspective of the federal agencies of like well we've said something, and it should be clear. But given, I think, we also need to think about communication strategy in light of the first

presentations that Oved gave, and Mary gave of just how stigmatized and confused a lot of the, and uninformed, a lot of the community, the medical community is. Like how do we break that down? And there are, there's some very large barriers of stigma. And so, we've got to go over and above.

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* I'm trying to figure out how we overcome those challenges one thing I'll say.

*Dr. Elizabeth Unger:* Okay. Thank you. Dr. Ling did you have another comment or is your hand left up from before?

*Dr. Shari Ling:* Oh, I finally figured out how to raise the hand. And so I didn't actually take it down.

*Dr. Elizabeth Unger:* Okay. And Mary is yours up from before or do you have something, another comment?

*Mary Dimmock:* The only thing I would add, and we'll probably talk about this more later, is that the federal agencies, their role is really important. But, when you think about how doctors, where doctors are getting their information from, they're likely getting it from their medical associations, from the institutions they work in, etcetera.

*Dr. Elizabeth Unger:* Yes.

*Mary Dimmock:* So the federal agency can do certain things to help with communication. But I think one of the biggest things that they can do is use their political capital with these organizations to get these organizations to be communicating to their members, clear, concise information that refutes the misinformation about the disease and helps them understand how to diagnose and treat it.

*Dr. Elizabeth Unger:* Thank you. Yes. And Ken did you have a comment? And, then we'll go for break after this. Sorry you're on mute. In my screen, if I take my cursor down to the bottom you get, there's the microphone to unmute. Well maybe, ah there you go.

*Ken Friedman:* Can you hear me okay.

*Dr. Elizabeth Unger:* Yes.

*Ken Friedman:* So, I'm here. Okay. So, I'd like, if possible, to have some thought given to stigma and possibly a more organized or more robust response to stigma when it is encountered. I can give you two personal examples. I and Andy Selinger recently submitted a paper on diagnosis and treatment of ME/CFS to a journal. And, the journal editor, even though the paper finally got through peer review, rejected it with the comment that she had heard.

[Inaudible/video and audio breaking up]

*Dr. Dr. Vicky Whittemore:* Ken this is Vicky, you're breaking up. Maybe if you turn your camera off, we can hear you better.

*Ken Friedman:* Sexual childhood abuse.

*Dr. Elizabeth Unger:* Oh dear. So now we're on the, let, perhaps let's take our break, and Ken we can finish your comments. And, maybe Monica, you and Ken can work together to see if there's something we can do to get this, to get him a little bit clearer. We did, I do think everybody needs to stretch and take a few moments. And we are due to come back at 2:55. So it's going to be a quick break so I will amend.

[Screen flashes to indicate a pause in recording]

*Ken Friedman:* Okay. So, what I wanted to say was that I would appreciate and if one wanted to overcome stigma, perhaps this is some way that we think about some sort of more organized or a response to stigma when it is encountered in the academic workplace. My situation was that in 2010 I received an email from my chairman stating that my activities in the field of chronic fatigue syndrome, which at that time Beth you know is essentially, I did some work for the CDC at that time or prior to that time. And, I was then working with Dennis Magnen on the NIH Chronic Fatigue Syndrome State of Knowledge Workshop, which we held in 2011, I believe. I was told that my work in the field of chronic fatigue syndrome was unprofessional.

And I could not find anyone who would stand up to that comment. And rather than give up that work, I decided I would retire rather than do that. But I don't think there are many

other people who would be willing to do that. So, if there was a way for some organized or stronger insistence that, when such kinds of comments or such resistance such as chronic fatigue syndrome or ME/CFS now is unprofessional, or that ME/CFS is triggered by childhood abuse, if there could be some more organized response or authoritative response, it might help.

*Dr. Elizabeth Unger:* Yeah. Okay. Yes. I will say we are definitely aware of the issue of stigma. And Vicky and I both joined NI, the trans agency working group on stigma to understand how stigmas are being approached in other illnesses. And we prepared a presentation for the stigma working group about ME/CFS and the kinds of stigma phase. So that is just a beginning. But, at least, at least we're understanding, we're learning more about stigma research. I didn't actually know that there are studies about how to minimize stigma and how to address it. And language and words matter tremendously. And so, we have got to be very aware of how we speak to each other, how we speak in the literature, and it's very important.

[Slide shows title page] And, so now, I really appreciate everybody's presentations. And everybody, the first part was supposed to be presenting a problem. But, in addition to presenting a problem, everybody had suggestions and thoughts about how to solve the problem, which is great. It is difficult to take the two apart. But I did want to, at this point, talk about some current initiatives that have been tried and are being tried. And, because then that frame what we could do next. So, in other words, if we're already doing some things, do I need to do them more, do we need to stop, do we need to amplify, etcetera. And so, I am going to start with what CDC has done. And, then Dr. Vicky Whittemore's going to talk about NIH's K Awards of Fellowship, which is only one tiny, tiny aspect of what they are doing. But again, we're focusing on largely educational and workforce development issues right now. And, then I asked Dr. Selinger to talk briefly about his experience introducing ME/CFS into the medical school curriculum. And, then I asked Dr. Erin Maughan to present about the work that the National Association of School Nurses has done related to ME/CFS and education. Okay. So, if we could have my first slide.

[Slides show key talking points] So, I'm going to focus these remarks on the activities we have done largely since the publication of the IOM report in 2015. Can I have the next slide? So, I just need to assure everyone that CDC's ME/CFS has been really very much aware of this problem and the need for improved healthcare and for clinicians that understand ME/CFS for quite some time. And we've developed activities to educate healthcare providers, particularly those in primary care. And the reason is they are usually the first to encounter patients with ME/CFS and their families. However, we also consider additional audiences including public health professionals, the general public, and patients and their families, as we've learned that educated consumers of healthcare can help guide their healthcare providers to educational resources. We've used as many different channels or methods as possible to reach this broad audience. Next slide.

[Slide shows images of patients and doctors and the key talking points in bullet form] One of the, one of our biggest activities related to CDC's public health Grand Rounds, this is sort of our bully pulpit for getting information out to public health officials and health care providers. The Grand Rounds, CDC's public health Grand Rounds have a strong reputation in the community for providing concise vital information. The topic for these monthly sessions are selected through a very competitive process. And we leverage new information in the 2015 IOM report as the rationale for holding this session. It was a significant accomplishment as it indicated CDC full commitment to addressing ME/CFS. It was a one-hour session with four speakers. It occurred, participants could view the session live in person as well as webcast and it was also archived online. CME was available for two years. The Grand Rounds material was also published in the Mortality, Morbidity, and Weekly Reports with CMM, with continuing medical education available. The MMWR is a series prepared by CDC often called the Voice of CDC. And it's one of our high, most highly accessed publications.

Finally, as an interview with one of the speakers, Dr. Anthony Komaroff, was available as a video clip in Beyond the Data. And these archived materials are still available at the links below. I have the next slide?

[Slide shows key talking points in bullet form] CDC has tried a variety of continuing medical education formats. And, most recently, we partnered with the Medscape. That was because they have the infrastructure to direct this material to specific medical audiences such as primary care. And they can also direct it to specialty care. Currently, we have three different course formats available. A round table video presenting information through conversations with experts. A case-based learning module that uses actual clinical presentations to direct learning. And a test and teach format engaging learners through questions to test their knowledge. Medscape materials are available free. There's no cost to use them. Medscape also produces expert commentaries from CDC speakers, and we use this opportunity to encourage clinicians to diagnose ME/CFS. And, this was, this is available still on our website.

The MedEdPORTAL is a publication of the American Association of Medical Colleges that provides educational resources for medical school curriculum. Our initial product that we published there focused on the important basic skill of patient interviewing using a poorly handled interview of an actor portraying a patient with ME/CFS, that's called the standardized patient, to educate about ME/CFS and to educate new clinicians about the patient interview. Again, we targeted the patient interview as a way to broaden interest of the healthcare community.

We sponsored two professional organizations to provide continuing medical educations to their members and provided consultation to third parties about their online information. And there, as somebody noted, getting medical professional organizations to educate their own providers, we thought was a way to try. Next.

[Slide shows key talking points in bullet form] The field of ME/CFS is at times filled with misunderstanding between all stakeholders. Anything that prevents anyone from moving together in the same direction is a barrier to progress. To provide a forum for the various stakeholders to hear each other's voices and thoughts, we've conducted two round table meetings. These round table meetings were each preceded by small group calls like mini focus group and then we had the in-person meeting.

At the meeting, the groups were divided up into tables including diverse representation to enrich the dialogue. In 2016 the main question was how to induce the IOM clinical

case definition, and in 2018 the focus was how to identify needs for health educational materials for patients and providers and to develop content for these tool kits. We also sponsored the Stakeholder Engagement and Communication Call since 2012. The mode in presentation in these calls have been evolving and we've been improving access, but the same format has basically been used. A brief content, a brief introduction of CDC's work followed by a presentation from an outside expert on a topic of interest to the community. And, finally, a question-and-answer period. The next slide.

[Slide shows key talking points in bullet form] CDC's website is intended to be a web, a resource for all. It is freely available, and we hope that all federal agencies will feel free to link to it and to use content. We've translated this website into Spanish to improve our outreach to this population. The website was developed with substantial input from all stakeholders and is continually updated. Next slide.

[Slide shows thank you] So I just wanted to thank all members of CDC's ME/CFS program for their excellent work in this, in this area and to my division leadership for their support. We think that consideration needs to be made as to how to make these activities sustainable. We see a lack of interest on the part of healthcare providers as a barrier that we cannot overcome alone. And one of the, I think it was Lily Chu's comment was CDC can't do this alone. That is absolutely true. We need, we need to collaborate and work together. As noted by several speakers, and as we're going to be discussing tomorrow, recognition of Long COVID is has brought much needed attention to the field of post infection fatiguing illnesses. And we look forward to continued work. Thank you.

That's all for this slides. And, so could we switch to Vicky's? And, then after, I guess after all of them we'll be having time for discussion and questions.

*Dr. Vicky Whittemore:* [Slide shows title page] Thank you Beth. Could I have my slides please? And while my slides are coming up, I would like to start by saying thank you to everyone who's participating today. I think hearing form all the stakeholders is critically important. And as Beth just said, it's going to take all of us working together to make these changes and make progress.

And, what I'm going to talk about today are NIH grant mechanisms that really are in place to help build clinician scientists. These are not certainly the only grant mechanisms at NIH. But, as Dr. Koroshetz also pointed out, this is just only one small piece of how we can help influence the development of new young investigators who are also clinicians and can learn about ME/CFS and provide healthcare to individuals with ME/CFS. So if I can have my next slide please.

[Slide shows NIH campus and key talking points in bullet form] So as I'm sure you all know; NIH is made up of 27 different components called institutes and centers. And each has its own specific research agenda often focusing on particular diseases or body systems. I am, as Dr. Koroshetz is the director of NINDS, are in the neurological disorders and Stroke Institute which focuses, as the name implies, on neurological disorders. So, each institute has what we call an intramural component which are the labs that are on the NIH campus or in some other locations in the country where research is actually taking place like the intramural group at the NIH Clinical Center that are carrying on the intramural study on ME/CFS. And, then there's the extramural component which is the group that where I work at NINDS that supports research grants to investigators at all levels of career development throughout the United States and often in foreign countries as well. And, then the next slide.

[Slide shows image of people in a meeting and key talking points in bullet form] All the program directors with an interest in ME/CFS participate in the Trans NIH ME/CFS working group, which was restructured, excuse me, in 2015. And we coordinate research activities across the NIH. So, it's chaired by Dr. Koroshetz and its composed of representatives from 23 institutes, centers, and offices. So, the program directors on the Trans NIH working group from the institutes are available to talk to investigators to assist with the grant application process as well as to really try to think about how to advance and stimulate and support research on ME/CFS. The group also includes representatives from the Center for Scientific Review. And you can see a list of the individuals who are on this Trans NIH working group, if you go to this link. And, then the next slide.

[image shows images of researchers in a lab and career development steps in a graphic] So all of the institutes and centers and all of the program directors on the Trans NIH working group are well aware of this path of career development that is supported in institutes, in all of the institutes at NIH. So, we support research all the way from undergraduate and post baccalaureate education through pre-doctoral training, post-doctoral training, through to, sorry, the chat pops up and then I can't see my slides, to early research career development, and then in this investigative development and in career development.

So, this is the career development phase. Again, as you all know, we also support peer reviewed research that comes into the NIH as investigator initiative awards from junior as well as established investigators. And, in the next slide.

[Slide shows key talking points in bullet form] I'm going to specifically focus on K Awards for clinician scientists since the focus of today's discussion is on building health, the healthcare professional workforce. So, career development awards are awards for candidates who wish to further develop their careers in biomedical, behavioral, and clinical research. The applicants are generally required to hold research or held professional doctoral degree or its equivalent. And eligibility in some, for some of these awards may be limited to only those with the held professional doctoral degree, for example, an MD, but not all. And it provides protected time for clinician scientists so they can focus on research while also performing clinical duties. And it provides support for basic or clinical research studies. So, at NINDS, we have a very hefty number of, if you could go back, please, we have a hefty program in our training office that supports numerous K awards across the neurological diseases. And I oversee many of these K awards in the epilepsies which is other area of research I cover.

As far as I can see, the NIH has never received an application for a K award. And so that is telling in that the academic physicians who are in the departments are not encouraging young investigators to apply for these kinds of awards where they could begin to develop their clinical or basic research studies while still seeing patients and learning about clinical care for individuals with ME/CFS. So, in the next slide.

[Slide shows names of awards and lists details of each] This is a run-down of the various K awards. And, not to bore you with going through each of these in detail. I'll just say that there are many different career awards, career development awards, that can help to support investigators in those early stages after they finish their medical training. So many of the K awards that come to NINDS are K08s or Mentored Clinical Scientist Awards where it provides the opportunity for the individual to have a training and mentored period of time where they can begin to develop those research skills before, they go out to become independent investigators and clinicians. There are others that are, as the K23, that are specifically oriented toward patient oriented research. So, it's not all basic research, it can be focused on clinical research. And so, there are many different ways, and different opportunities here for individuals, even the K24, which is a more mid-career investigator award for clinicians who want to do some research to get these kinds of awards at NIH and to be supported. And again, what this allows is protected time for the individual to develop those research skills. So, the next slide, please.

[Slide shows different levels and some description] The other avenue is what we call the early-stage investigators. And these are program directors are investigators who've completed their terminal research degree or the end of their post-doctoral clinical training, whichever dates later, within the past 10 years who've previously completed, successfully, who have not, sorry, previously completed successfully for an independent, like an RO1, or an independent NIH grant, to submit RO1 equivalent grants, and when they're funded to go on to develop those careers. In most institutes at NIH, there's a significant bump in the pay line for these early-stage investigators. So, for example, at NIMDS, our pay line went up, the pay lines at the 14th percentile, we look at and evaluate and fund early-stage investigators almost 10 percentile points above that pay line. So, it really is a way in which early career investigators can also, basic scientists and clinical scientists can really launch their careers, as well. And the next slide please.

[Slide shows key talking points about program director] So, I'll just end by talking about what a program director does and how we can help. And so we are, as I said, in the

trans NIH working group, there are 23 individuals represent the different institutes and we are ready and available to talk to investigators, at all levels of their careers, to provide information about funding opportunities, what's the best grant mechanism, to help you review the specific aims for your grant applications. We then listen to the review and discuss the summary statement so we understand if the grant does not score well, what were the, what were the key weaknesses, and how can you improve your application. We helped investigators answer questions and navigate the NIH system. And then of course, we administer the grant when it's awarded.

There is a matchmaker tool on the NIH website, so if you're studying the immune system, neurology, and ME/CFS, GI system, you can go to matchmaker and it will identify individuals who are, have grants in those similar areas that you're interested in exploring. And then the next slide.

[Slide shows email address] If all else fails, you can contact me. I'm ready and available, and I have to say, probably in the last 3 months, I've had conversations with young investigators, as well as established investigators in ME/CFS at least two or three a week. So, I think the gratifying thing in the research field is the various growing interest. There is growing awareness of the opportunities available at NIH for, to support research on ME/CFS and growing awareness that we are very interested in supporting this work. An awareness that we, as program directors, that's our job, is to help investigators. And the bottom line, here, is that I think we need to reach out to the academic centers and make them, help to make them aware of the significant need to build this pipeline of investigators and that one way can do this is through these K awards and these career development awards. So, I'll stop there. And thank you, Beth.

*Dr. Elizabeth Unger:* Thank you, very much. That's great. So again, we'll have more time for discussion after these presentations. And but I'm, Dr. Selinger, are you at a place where you'll be able to do your presentation?

*Dr. Howard Selinger:* Yes, I am.

*Dr. Elizabeth Unger:* Okay. And the presentation will be advanced by Monica, so you just have to let her know when you're ready to move to the next slide.

*Dr. Howard Selinger:* [Slide shows key talking points in bullet form] Well, you can move. We're going to talk about ME/CFS at the undergraduate medical level. Hopefully you can all hear me. I'll take the next slide. So, I chair family medicine, the Frank Netter School of Medicine. The school was started by a donation from the famous anatomist's estate, Frank Netter. We're a new breed of medical school, launched in 2013, graduated our first class in 2017. You need to understand that unlike your typical image of a healthcare center, all clinical training happens in the community, both ambulatory and inpatient. There is no faculty practice, there is no onsite university medical center. And at this time, there's no robust research. It's all about teaching at the undergraduate medical level, which has its pros and its cons. This was done to not compete with the medical community. But obviously, as was talked about earlier, we do not have a robust research infrastructure and your classic academic clinician.

Our class size is 90 to 95, not insignificant. And I need to be transparent with everyone, that this curriculum would not have happened if we had not been funded by a very generous octogenarian who has lived with ME/CFS for many years and made a six-figure contribution to endow the chair of family medicine, matched by the medical school, with the request that we create an undergraduate medical curriculum. And that is why we created an undergraduate medical curriculum.

There were no barriers encountered, which by that I mean it doesn't go through curriculum committee on oversight. And let me tell you, curriculum, there's a lot of turf battles that go on as what's going to get accepted as curricular content. We were able to move this through ancillary departments within the medical school, rather than the basic foundations of medicine. And that is what enabled us to offer first year, second year, and third year onsite training in ME/CFS. I'll take the next slide. Next slide.

[Slide shows definitions of different levels] So, what we're looking at here is in the first year, you've got young medical students, they are still well aware of their lives outside of medicine. And so, we present to them patients and families, they're living with this on a daily basis. Our goal is really to humanize the experience for students. The experience, go ahead.

*Dr. Elizabeth Unger:* Sorry. Monica, I think she's one slide ahead of you.

*Dr. Howard Selinger:* [Slide shows table breaking down medical school year and curriculum] Yeah, can you back up please? I'm still going to verbalize that that is our goal, but I'll back up. So, our goal is to humanize this for our students who are still receptive to the humanity involved in dealing with chronic illness. I hate to say it, but that receptivity tends to diminish over the course of 4 years of medical school as you are forced to engage with a more rigid healthcare system.

In the second year, we really focus on objective structured clinical reasoning, as described here, where you have to consider a variety of differential diagnoses, of which ME/CFS is one. That means you introduce a patient, with a standardized patient who has a script around why they're there, what they're suffering with, what they're clinical concerns are, their chief complaint. You go through an examination, and the second-year students are expected to consider, based on readings done prior to this session, ME/CFS, among other things, that are equally significant in producing fatigue, or unrefreshing sleep, and practice the ability to distinguish different diagnoses from one another.

In the third year, what we basically do is offer a straight didactic, as our students are now out in the community rotating through inpatient and outpatient programs, and this, I'll show you some representative slides later, but this is an opportunity to drive home the recognition that you don't always have clear cut criteria and clear-cut diagnostic algorithms and treatment algorithms out in the real world with real people. These three years have been deployed.

The fourth year would have been deployed, but the pandemic hit, and that's a funded 4 week away rotation, for anyone who wants it, at one of the ME/CFS centers throughout the country. We hope once the pandemic restrictions are lifted to be able to locate students who would be interested in that. Take the next slide, please.

Right. And I've already said that about medical education often deemphasizing the patient's centeredness focus. Next slide please.

[Slide shows curriculum focus] So deductive clinical reasoning, hypothesis driven in the second year, which I've alluded to. Next slide.

[Slide shows curriculum focus] And in the third year, I want to show you some representative slides of every student rotates through a primary care clerkship so that every student in each of these years is exposed to this perspective on a complex clinical condition that is not easily codified. Next slide, please.

[Slide shows list of expectations] So, to give you an idea of what we stress, and this is obviously my department, and the students rotating through, we really try to push the point. Just as it says here, be a detective, be a clinician, don't roll your eyes. And then we try to make it very relevant to the current times about how there are many similarities, expressed by Tony Fauci and others, between COVID long haulers, and how that's going to magnify the numbers of people that may fall within this diagnostic and clinical category exponentially. Next slide.

[Slide shows breakdown of doctors and patients by percentages] Again, we share with the students, here's what patients suffer through, how many doctors they need to see. And again, these are third years, out in the community, in their primary care rotation, which is ambulatory. Next slide, please.

[Slide shows language that should and should not be used] And here, again, we try to drive the message home. It is not psychiatric; it is not deconditioning. Don't do the exercise by just, you know, all these things which are counter to what some students may think is appropriate. And this lecture, this 60-minute lecture also includes the diagnostic criteria, the NASA Lean Test, the post-exertional malaise, staying within your energy envelope, some of the medications that are used to mitigate the symptomatology. So, because they're third years in the community, we want them to understand what it's like to have hands on, and we have not yet been able to query them as to how many may have actually believed they've seen this. Next slide, please. Right.

[Slide shows Osler quote and tips listed] So as Osler said, listen to these patients. And we stress the patient's centeredness in the primary care rotation. It's, you know, the exam is often used to validate the history. And again, this message of don't have premature closure in your thinking, keep your thought processes open, be deductive,

but don't close the door on what you believe to be going on. And finally, last slide, I believe.

[Slide shows fourth year information] And that alludes to what we hope to launch once things are opened up again for interested fourth year students. And the key here is, you hear about it in year one, again in year two, again in year three, so the longitudinal re-exposure is what's so important. And I'm told we're the only school doing this, but you also need to recognize the limitations of a school like ours, where there's no onsite university academic medical center. It only just started right prior to the pandemic, and hopefully, well this spring will be our second M1, and we, probably our third M2 next fall, and our ongoing M3, because those students are rotating through, this year every 4 weeks because they were not out in the clinical setting, in the future every 6 weeks. So that's what we're about at the undergraduate medical level.

*Dr. Elizabeth Unger:* Thank you. And could you comment if you had to go to the curriculum chairman or to get approval to do this.

*Dr. Howard Selinger:* I honestly think pre-COVID we would have been turned down and said we're sorry, there's not enough capacity in the curriculum to accommodate this disease, because it's very, very hard to break into the formal curriculum. But when you do it in a way that's rotational based in the third year, or clinical arts and sciences, which is a separated department in the second year, or SRCC, which is another second afternoon evidence-based medicine department in the first year, you kind of skirt the curriculum committee on oversight.

*Dr. Elizabeth Unger:* Right.

*Dr. Howard Selinger:* That's exactly what we did.

*Dr. Elizabeth Unger:* Yeah. And when I talked with you earlier, I thought that was a very ingenious way to do it. You can incorporate it without specific approval.

*Dr. Howard Selinger:* Right.

*Dr. Elizabeth Unger:* Just, yeah. So, Nancy, if you have a quick comment, then we need to go to Erin. You're on mute.

*Dr. Nancy Klimas:* I was saying that case-based learning is very common now in medical curriculum, so we provided a case for the case-based learning section of the freshman year curricula. And that was very well received. And now it drives a lot more people into our elective.

*Dr. Howard Selinger:* Right. In our first year what we did is we, part of this afternoon session included the students, they were required in a collaborative classroom environment to look up various clinical question directly related to ME/CFS. The goal there was how does one learn to research the evidence, and then present this to the group as a whole after the patient and family exposure, which occurred in the first hour. That was the direction we chose to take. And I guess the case based would be the OSCE, the observed structured clinical exam, in the second year. But then again, that's more deductive reasoning.

*Dr. Elizabeth Unger:* Okay. Thank you. And could we move now to Erin Maughan, who is representing the National Association of School Nurses.

*Erin Maughan:* [opening slide shows young people in a classroom and title page] Wonderful, thanks. Thank you so much. And I appreciate this opportunity to share what we've done. I've also appreciated hearing from those of you who suffer from ME/CFS and getting that patient perspective. It's extremely helpful. So just as a little bit of background, the National Association of School Nurses is a membership organization. We represent all the nurses that work in both public or private schools, mostly kindergarten through grade 12, but many schools are beginning to have a pre-K program, and we welcome them, as well as members.

We have about 17,000 members in our association. But we also, part of our mission, which is to optimize student health, is to push out information to all school nurses, not just our members. Each of our, each state has a chapter, we call it an affiliate, that has local leadership, and we use that network often to try and get information out to all school nurses, not just our members. I thought also to, oh, if you could advance to the next slide, please.

[Slide shows a color-coded image of the country illustrating the breakdown of nurses along with percentages] I thought it might also be helpful to kind of share how school nursing is in the United States. You may or may not be aware of this, but about 25% of schools do not have any type of school nurse. That's the bad news. The good news, though, is that 75% do have a school nurse. It might not be full time, and it really depends a lot on where in the country you are will depend on if that nurse is full time versus part time or not at all. It also influences their education level sometimes, be it if they are a registered nurse with at least a baccalaureate degree, that is our recommendation from the National Association of School Nurses, or if they have an associate registered nurse degree. Or in the south, I will say there seems to be a little bit more of a licensed practical, or licensed vocational nurses working in the schools. And we're glad that there's nurses. We try to, we welcome all and try to get the information out to all of them.

So why Dr. Unger had asked for me to speak today was, I think, because of a program that she's alluded to where we've been really trying to increase the surveillance of our school nurses to watch for ME/CFS. And part of that program is to provide education to our school nurses. Advance to the next slide, please.

[Slide shows two people talking and talking points in bullet form] I just want to share the process that we followed. So, the program started about, in 2018, and we, the first question we asked was had school nurses heard of ME/CFS and the far majority had not. So, this kind of supports, unfortunately, what I've heard in the discussion today about it just, people aren't aware of it. And it literally took that to heart because one of the barriers, and I'm a former school nurse, loved being a school nurse, but I definitely think one of the barriers is once out of school, it's really upon the school nurse, or nurse in other profession too, to keep up to date on information. And I know ME/CFS has been around for a while, but there's also been new advances. And if it's not on someone's radar, it's very difficult to know to make sure they keep up with the data on it. So, we need, first and foremost, we needed to set the context of what ME/CFS was, in order the school nurses also were more likely to be receptive to it. As one of the speakers spoke this morning, the providers, those that seem, if I understood correctly,

those that were more receptive were the ones that had some type of a personal connection with ME/CFS. So, I think that's true, too.

Luckily when this program started, the documentary Unrest was on Netflix, so we actually really tried to promote having them watch that to understand really what it was like, and understand the science, and sometimes just how debilitating it can be in one, in a person's life, to kind of start the context for additional education.

Because of the surveillance program, we have a state data coordinator in each state. It's a voluntary position. And we started with them because they work with their affiliates and are able to push information out. Again, we did a needs assessment for them, and they hadn't heard about ME/CFS, so that was really important. Using the information that CDC has, which is wonderful for schools, we promoted that information. We actually promoted the Medscape CME course that was mentioned earlier, as well. And then we had a breakout session at our 2019 conference that was recorded was made, then made into a webinar that is still on our website, and we still continue to promote that. We have training sites for our surveillance group, and we also did specific training for them in those local areas.

We picked, or we chose states that have specialists in ME/CFS, so we provided the information on who those specialists were and encouraged them to connect locally with those organizations so that, because the pilot sites we're looking specifically to identify students that may have undiagnosed ME/CFS or diagnosed. So, we tried to connect where we could.

A little bit of information that I thought might be helpful, I just want to make sure, oh and the other thing, yes, I apologize. One other thing that we do from an educational perspective is we have a weekly electronic digest that goes out beyond our members. It goes to about 35,000 school health interested people, including school nurses. And we pushed information there, as well. Just a lot of is just trying to get the awareness.

And for school nurses, it's helping them identify what the signs and symptoms are, so that they are aware, so that they can work with parents who may or may not be aware to even consider ME/CFS, and then to help them link into a specialist, and to work with

parents as much as they can, also, in addressing things on the school side. I saw one of the patient quotes was, the frustration found working in schools. And unfortunately, we have heard of that as well. On the flip side, we've also heard, well, we should back up to say context is part of it. I think some of the rules on how chronic conditions are managed in schools, it's very much based on having an official diagnosis.

And I think from this program, we've learned how difficult that is, because for children or students, at least 6 months. And so, one of our pilot sites, although I will say we haven't found any students with ME/CFS that have been diagnosed, or been identified because of our program, it might, anyway it's a long story, I'll talk about that if you're interested. I'm sticking on education here. But the point is, we have been able to work with districts in preparation, and that in some districts they are able to work with their home and hospital, which is often times with a diagnosis, but can be for other things, too, to help try and coordinate and work with students even before they have diagnosis. Because, like I say, that's the traditional way school nurses and school health is addressed, is by diagnosis, and that's not always possible.

I know it's been mentioned a lot, but I would say silver lining, if you want to say of COVID, is definitely that it has increased, and we've tried to highlight, the various information about COVID being connected with ME/CFS and the importance for school nurses to be even more on their toes to help identify symptoms and to talk to parents and families about that. To work with them from the school level if they're in schools, many of them are virtual right now, as well as, like I say, helping get into further treatment and diagnosis so that further treatment can be identified. We're hoping, we'll continue to push that, too.

We also have a case, it's a chronic condition management manual that's coming out. And in that, we've included a case study specifically on ME/CFS undiagnosed, first, in another attempt to try and help school nurses know what kind of questions to ask, what kind of things to look for, that kind of information, in hopes that, well since we know so many don't know what ME/CFS was, we pushed that first. And now, like I say, we also want to give the tools to school nurses, so they know what to look for.

And then with that, just a little bit of information, we did do an evaluation on those that have participated in the webinar, and we're encouraged on a Likert scale of 1 to 5, 5 being the highest it can be, 4.5 felt like after the presentation and information that they felt confident in being able to identify symptoms that might be ME/CFS, so that's good. 4.39 felt that they had the tools to advocate for changes, as needed, related to ME/CFS. And 4.45, again these are all out of a Likert scale of 5, felt that the information influenced their practice, and they would make changes. So, we feel like that's going in the right direction.

But also, definitely feel a need to continue, and especially after listening today, and using the opportunity that COVID has provided in discussing it, in unfortunately that it might increase the rates. That we really need to make sure school nurses are in top of things in knowing what ME/CFS is and what signs and symptoms to look for, and to connect with a specialist in their area, and to know what this, how they can support students and their families, even before their diagnosis in addressing school issues. Especially because we also feel that there'll be an increase in anxiety, school anxiety, which often times ME/CFS is misdiagnosed, and they put it to that. And so, we do want to address the anxiety, but we don't want that to be stopping the situation, in that they really look into to make sure that the correct causes and symptoms and condition is diagnosed so that proper treatment can be given. And that is all. Thank you.

*Dr. Elizabeth Unger:* Well, thank you so much. So, if we could, are there any questions or comments about these last four presentations, before we open up for general discussion?

*Christine Pearson:* So, Beth, we do have, we do have one question, which is what inspired NASN to implement this ME/CFS education program?

*Erin Maughan:* Sure, it was actually because we received a contract from the CDC to do it particularly. And I'm grateful that we did, because it wasn't on our radar like it should have been. So, we appreciate the opportunity.

And I don't want to take away, but since I'm answering, if for those, I would love if, in the chat because I don't want to take away from discussion, but would really appreciate

those that have worked with schools, any feedback or information that would be helpful so as we move forward we can make sure that the school nurses better understand, maybe, what questions to ask or if they're aware of how things have, people have felt mistreated or not gotten the attention they need, how we can address that better. So, I just wanted to throw that out, as well. Thank you.

*Christine Pearson:* Okay. Great. And there's actually a couple of more for you, as well. Can you restate the number of school nurses reached to this point, and the locations of the nurses? Thank you for this great initiative.

*Erin Maughan:* So, I think maybe, so there's kind of two parts, but pilot sites, that's where there's a specific reach in that they're working in 6 different districts. Two of them are in Utah, one is in Florida, one is, or two are in Michigan, I'm sorry, and one is in Massachusetts, districts that are working on it. And I will say, we had, this was the year that they were supposed to really expand both in the districts we were working with, and beyond those districts, and COVID has definitely impacted that, just the bandwidth. The original pilot nurses are still working, and we have expanded it some, but not like, just to one or two more. Honestly, because COVID was not what we expected.

In regards to the education, however, that has spun out to all our members, for sure, and beyond. So there are 17,000 school nurses who are members of NASN, but our information has been pushed through our affiliates. It doesn't necessarily get to every single one, but it gets to many, many more than that.

*Christine Pearson:* Okay. And then we have three more for you. Have you experienced any push back among your regional physicians' support?

*Erin Maughan:* No, we haven't. In fact, I will say, I reached out to, I gave it, when we were doing this, I gave the choice to our pilot sites if they chose to reach out, because some of them actually had already had connections with their specialist, or if they preferred me to kind of do the initial. And the ones that I did the initial for, I actually got a very nice response back with willingness to help however they could. And then I linked them into the pilot sites and let them take it.

We've encouraged them to have presentations at their state affiliate meetings. Again, COVID has kind of messed all of that up. So, I can certainly re-encourage, because a lot, even last year, they're usually in the spring, and even last year many of the conferences were canceled due to COVID.

But no real push back from the providers, that I have heard, at least. Most of them have been, from what I have heard, kind of like many of our, the specialists, of course, know, but some of the primary providers have also not really heard of ME/CFS, and so that's what the school nurses have indicated. We use the fact sheets that have been so nice, that CDC created, and we encourage the school nurses to share those with providers and families to help educate. And we've heard positive feedback that they weren't aware of it, so they appreciated having it on their radar.

*Dr. Elizabeth Unger:* Great. Thanks. Nanda, it looks like you have a, would like to make a comment. We're not hearing you. Did you try again? Well, Monica, maybe you could help Nanda sort this out? Because she's going to be giving a talk fairly soon, so we have to be able to hear her. But meanwhile [Inaudible] Let's see.

*Monica:* Nanda, can you put something in the chat, if you can hear us? Because it looks like your audio is connected or else trying to call into your dial in line? Oop, I can hear you fine, okay. Okay, so let's do this. If you can press the, it's either down or up arrow on your mute button and go ahead and test your speaker and microphone so I can find the output.

*Dr. Nanda Issa*: My question, or should I just go later?

*Dr. Elizabeth Unger:* Please, go ahead.

*Dr. Nanda Issa:* I actually had a question for Dr. Selinger. Thank you, so much for speaking about the integration of NCFS and the medical school curriculum. I was just thinking about how I also saw standardized patients, maybe more long ago than I'd like to admit, but in how much it would have opened up my eyes as a student to be able to evaluate a patient with ME/CFS.

One of the things that they used to talk about in clinical classes is, you know, if you hear hooves, don't always think of horses, it might be a zebra. And it's just, it just goes to say that it's not necessarily the first thing you think of that, in the differential that might be the actual problem. And I think it's a really great way to establish that narrative early on in their medical training to have that. And as you said, not to close the door, especially.

I was actually curious to know if the medical school is, or is planning to follow a cohort of those medical students over time as they, for lack of a better word, go out into the world and kind of watch for [inaudible] about ME/CFS?

*Dr. Howard Selinger:* At this time, there's been no plan to do a post graduate evaluation. That's a very nice idea. You know, everything's been derailed by the pandemic. That had not occurred to us. We were barely able to get this launched.

[Inaudible]

*Dr. Nanda Issa:* Oh, I'm not able to hear him. But. Yeah. Like he said, that maybe later on they'll do it, but they can't because of everything that's going on now.

*Dr. Elizabeth Unger:* Yes. Yeah. Okay. And Dr. Selinger, I'm sorry, you were cutting out, and maybe dropped off entirely. So maybe when you log in, if there's another, he can comment a little bit later. So.

*Dr. Howard Selinger:* Can you hear me now?

*Dr. Elizabeth Unger:* Yes, yes. Go ahead.

*Dr. Howard Selinger:* Yeah, I'm sorry. I just said that it's still considered a diagnosis of exclusion, even amongst clinical colleagues, and even when you front load a clinical case with very clear diagnostic criteria, antecedent viral illness, post exertional malaise, unrefreshing sleep, there's still this attitude that you've got to rule out every possible organic etiology before you then begin to consider this. So that's a battle we still need to fight.

*Dr. Elizabeth Unger:* Okay.

*Dr. Nanda Issa:* Thank you.

*Dr. Elizabeth Unger:* Any other comments before we move to general discussion? And the idea of this discussion is to, you know, now you've seen what we've done, what has been tried, and what are the next steps that we should take together, what are some suggestions, and that's what this workgroup is supposed to really do. So, anybody want to start? We could maybe go back to Oved's slide, which had some discussion points on. And we're, yeah, we're going to leave a little bit of time at the end. We do want to review where we're at with the systematic review and NIH's plans for a workshop, so. But and I, and Christine have we been sort of answering the questions as we go along or are there a lot more?

*Christine Pearson:* Some of them.

*Dr. Elizabeth Unger:* Okay.

*Christine Pearson:* I think, some that have been directed at specific people. Like I see Erin is going in and doing a few. As I mentioned we are, we're noting down the ones on long COVID to address tomorrow. But there are still quite a few.

*Dr. Elizabeth Unger:* Okay. Okay. Anyway, anybody want to start with some comments.

*Dr. Howard Selinger:* I will start. I just want to say, as a practicing primary care, boots on the ground, family physician, and now teaching students and residents, I think we have to acknowledge that we won't make actionable change, at least in this regard, until we link the new reimbursement approach with its focus on time and complexity to a disease like ME/CFS and get the word out there so that it penetrates the minds of busy primary care physicians who really aren't thinking about it. And most of them are now owned by hospital systems and healthcare insurers, not all, and drive the message home that this does not have to be a financially losing proposition. As crass as it sounds, I think it's going to be an essential element.

*Dr. Elizabeth Unger:* [Slide shows question and answer suggestion bullets] Yeah, so that's, in a way, addressing some of the structural barriers, which is reimbursement and, you know, how can we, what sorts of clinical approaches are more effective. Dr. Koroshetz, you have your hand up?

*Dr. Walter Koroshetz:* Yep. No, I really appreciate hearing all the efforts that people have taken in realizing how tough it is. It's possible that one silver lining to the epidemic is that many of these issues with regard to the care of people with ME/CFS may dissipate. I say that because in preparing the research for post COVID syndrome, we've been talking to doctors from all over the country, and most hospitals now are actually starting clinics particularly for people who had COVID and are not better. And the [inaudible] in symptoms is pretty dramatic. So, people, most of the people who are running these clinics, you know, had no experience with ME/CFS, but they are on a steep learning curve. And they will be, you know, within a year or two, a cadre of medical professionals that could be really, really helpful in helping to take care of people who have ME/CFS who, you know, did not have COVID.

*Dr. Elizabeth Unger:* Right.

*Dr. Walter Koroshetz:* I think that's one, we're in a special place now. I mean, it's terrible about the pandemic.

*Dr. Elizabeth Unger:* Right.

*Dr. Walter Koroshetz:* But there is certainly a possibility that this could be a game changer for those who are suffering with ME/CFS.

*Dr. Elizabeth Unger:* Yes. I've had more clinicians tell me, you know, will admit, well there's lots that we don't understand and have much more of an open mind. And one of the barriers that we've, CDC has sensed with our continuing medical education, is how to get clinicians interested. And the COVID is, and the numbers of patients with this kind of problem could be the impetus to get people interested. So now we've got a number of hands. So could we go to Charmian. I think maybe yours was first. Sorry if I'm calling out of order. And you're on mute.

*Charmian Proskauer:* This is funny, because I see Charmian, Mary and Ben, and I'm pretty sure we may all have the same comment. And from the ME/CFS patient perspective, the concern is that long COVID will be seen as a separate entity, all of its own, and that the symptoms will be what they are, and it won't matter that they are very similar or the same symptoms that people with ME/CFS are experiencing today,

ME/CFS will be left out of the discussion. And we'll be pushed aside and left behind once again. I think that is the key challenge from the ME/CFS patient voice perspective that we have to make sure that that doesn't happen, and that long COVID doesn't become its own thing.

*Dr. Elizabeth Unger:* Yes.

*Charmian Proskauer:* And ME/CFS fades away.

*Dr. Elizabeth Unger:* Yes. We, I.

*Ben HsuBorger:* Agree.

*Dr. Elizabeth Unger:* And that sort of is number, was that number 4, needed focus on long COVID leave ME/CFS patients behind again. We cannot, I agree totally, and the CDC has been doing what we can to emphasize that. And I believe the NIH language is very inclusive, as well. And we just need to keep emphasizing that, because the very worst thing that could happen is that long COVID is one thing and ME/CFS is another. And that the ME/CFS patients need to benefit from this. We were on a call with WHO about long COVID, and this is long COVID, not workforce development, and they said they didn't want to leave the long COVID patients behind, and all I could think of is, well we can't, you know, what has, the ME/CFS community has been left behind and we need to catch them up. So, I agree. So, Ben?

*Ben HsuBorger:* I'll let Mary go before me.

*Dr. Elizabeth Unger:* Okay, Mary. You can go ahead, Mary.

*Mary Dimmock:* Thanks, Ben. I was going to come back to what Dr. Koroshetz said. These long COVID clinics are being set up all over the place, and in a couple of years they'll know quite a bit. But we can actually expedite what they're learning by taking advantage of what these clinicians who were already treating ME/CFS have learned over the last 30 years. And doing that is going to require some sponsorship, some funding to support them communicating, but I can easily imagine a comprehensive program that would provide that kind of knowledge base that we already have up to

those clinics. So rather than it being 2 years, we actually have them treating patients the way we need them to in a year, or 6 months.

We do know, this is important because we do know that some of these clinics are recommending exercise, saying the patients are just anxious if there's no evidence of organ damage, etc. And so, I think it'll be really important to help them learn what's already been learned as quickly as possible. Thank you.

*Ben HsuBorger:* I'll just keep my comment really brief. Thinking back to what Mary said, from a, the negative lining that I would see, that any action has, you know Beth, we've spoke with your CDC team at the end of last year about this. But we've been tracking a lot of the long hauler press coverage, and the clinics that are popping up, and I would say I do not see that silver, that unfortunately I don't see that silver lining right now because I think it is very uneven. And there is actually, you know, I see actual harm that's potentially going on in long COVID clinics where ME/CFS people who have developed ME/CFS from COVID and not getting effective treatment for their disease. And so, I think that is Mary's points to what we can do about that are really important now, because I would say from the work, we tried to survey the ground, I would, I do not think all the COVID clinics are up to the knowledge of ME/CFS. So, the question is, what can we do to change that? Thank you.

*Dr. Elizabeth Unger:* Okay. And Oved?

*Oved Amitay:* Thank you. I just, I wanted to go back to Dr. Koroshetz comment. I think we do agree that there's a potential here to really make a difference, you know, the kind that we are all talking about the first part of the conversation today. But I think that ultimately that requires a really a coordinated effort. I think that we realize that the challenge has been very large even before COVID, and it's just a growing gap.

And you know, to Dr. Selinger's point before, of course it's important to teach medical students, and that's with the time to do that. Now in the past, it's possible that our physicians were not interested, or they didn't think that ME/CFS was something they should be aware of. With long COVID, that is no longer acceptable. And I don't think that's really going to be, really going to be true.

So, the question is how do we really have an effort that encompasses all those different aspects? And I think what we take from the discussion this morning is that it is all interconnected. Dr. [Inaudible] about the need for clinical research, and the challenging in attracting people to come to a clinic that doesn't have research opportunities. So, we have to address all of those aspects in a coordinated way. If we just let things grow organically over the next few years, I'm very concerned that we're going to see the problem growing even bigger than it is today.

*Dr. Elizabeth Unger:* Yeah. So it really is difficult to have a conversation about ME/CFS without getting into long COVID. But we are trying. And tomorrow is when we're really going to focus on long COVID and talk about how the agencies are working together, as well as with WHO, to try to address this and then is when we can focus more on how to make sure we get ME/CFS included with all of the benefits and the funding that's going to come with long COVID.

*Oved Amitay:* Let me just get one.

*Dr. Elizabeth Unger:* Yes.

*Oved Amitay:* One specific comment that I wanted to make. And this is to this question number 5, how can we do things differently?

*Dr. Elizabeth Unger:* Yes.

*Oved Amitay:* And I think that over the past year, we've all changed the way we work. We're now zooming. This conversation probably would have been done differently in a different.

*Elizabeth Unger:* Yeah.

*Oved Amitay:* But I've been following the emergence of this branch of e-consulting, which is really the way that organizations, many of them are for profit organizations, provide medical consulting to primary care physicians. I kind of think about it as, you know, Uber for medical doctors. But it's sort of this idea that you can use experts really specifically based on a physician's needs. There are a number of these organizations now, and that could be a very efficient way to educate many physicians in the primary

care setting by contracting those organizations. Similar to the way you did with Medscape and others. I think these are relatively cost-effective ways to educate a large number of physicians to something that, at this point, they would feel eager to learn more about.

*Dr. Elizabeth Unger:* And, whoops, yeah, Dr. Koroshetz.

*Dr. Walter Koroshetz:* Well, thank you. I think all good points. I just wanted to raise one other one, which I raise it with every disease advocacy group that we meet with, most of which have a very similar problem, maybe not as acute, but similar in not being able to find the caregivers that they need. And I just think back to how people's careers in medicines evolved, and I think that there are these tipping points in people's careers where, you know, for one reason or another they decided to go in one direction or the other. And I think that it's the experience that the young people have with the patients, and actually the disease organizations can have a tremendous leverage there. So, I think we can't really underestimate the power of the groups that are on the call today who represent the patients in their ability to convince people, young physicians, nurses, nurse psychologists, whatever, that this is a really important and needy area to go into. At the government level, we have basically zero leverage, to tell you the truth.

*Dr. Elizabeth Unger:* Yeah.

*Dr. Walter Koroshetz:* In terms of determining what people, what kind of careers they're going to go into. And just looking back to my career, you know, I really didn't have any, I didn't really have any expectations of going into one disease or the other, and I just ran into these people from the Huntington's Disease Foundation, and it was so compelling, you know, that I put my career into Huntington's Disease. A lot of stigma in those days, people with Huntington's Disease were locked up in their houses so that no one could see them. There was nothing that we knew about the disease. But it was really personal interactions with the disease organization folks that really made a difference. And I wasn't the only one who was really, a lot of other people went the same direction because of that organization. Do not underestimate what you guys can do to get people into the field. But to target the young people is the key. You know, once the people are out in practice, it's a tough sell.

*Dr. Elizabeth Unger:* So, I agree. And one of the, one of the questions raised here is what agencies need to be in this meeting that aren't here? And I do want to explain, we have invited others to join and right at the moment there has not been enough bandwidth for people from the FDA or AHRQ to join us, but we are reaching out to them. And I think it's important that we have as many of the agencies as involved as possible. We also got a suggestion from Charmian to include the Indian Health Service, which is a good idea. And we need connections often with these agencies. In other words, who is the right person to talk to, so sometimes it takes us a little while to make the right connections.

We do, one option to really try to come up with, you know, our ideas is like what should we, how should we, what programs should we do, what, how should we emphasize what we're doing, anything new we should undertake? And so, one of our thoughts was that perhaps we need to have a working, sort of, subcommittee of this to discuss offline some of these issues. In other words, we can't do everything today. That's just a suggestion. Let's see, so there's a lot of hands up, are they all. Dr. Koroshetz did you still have something new? No. Okay. Charmian did you have something new? Okay.

*Charmian Proskauer:* Yes. I just wanted to add HRSA.

*Dr. Elizabeth Unger:* Add HRSA, yes, okay.

*Charmian Proskauer:* If we, if we are going to make any effort, any realistic effort to reach out to any underserved communities, the Community Health Center Network is the way to go.

*Dr. Elizabeth Unger:* Yes. Yes. And we've actually, you know, I learned a lot by talking with some of the community health centers. And the constraints that they're under, and it's going to call for some really creative thought as to how we can develop systems that will allow for care of these patients, very complex patients under those circumstances. So, Nancy, did you have a comment.

*Dr. Nancy Klimas:* That was a good segue, because actually my question of the governmental bodies that are here is just how do we support the clinical care network, perhaps on the backbone of the clinical research network, or in some merged way? I

know right now that HRSA is about the only place you can send direct clinical money to, and yet that's going to be only working through these community care networks. Not that that's unimportant, that's incredibly important. But is there a way to be thinking more creatively on how we might actually be able to implement what has been the number one recommendation of the advisory committee for decades, which is to create clinical centers of excellence, so that we can roll this knowledge out into the field and train young doctors and encourage them to go into this career and so on.

*Dr. Elizabeth Unger:* Yeah. It's hard to do clinical centers of excellence when there's so few academics that have centers to even start.

*Dr. Nancy Klimas:* Oh, there's no funding mechanism

*Dr. Elizabeth Unger:* Yeah.

*Dr. Nancy Klimas:* Okay, I have a center. How do I do that?

*Dr. Elizabeth Unger:* Yeah. Yeah.

*Dr. Nancy Klimas:* Just explain it to me, because there isn't a way.

*Dr. Elizabeth Unger:* No, no. I'm just saying, you know, for just spontaneously, we need to solve the problem of getting academics in.

*Dr. Nancy Klimas:* We do. We do.

*Dr. Elizabeth Unger:* Yeah.

*Dr. Nancy Klimas:* But we can't do it by saying we need more without giving them a place to live. When geriatrics first came out as a field, it was a very underappreciated group. And so, the whole NIH Institute for Aging was born, and they created centers of excellence, clinical centers of excellence that had research cores and educational missions. And they created the field. But it was an NIH initiative that created that field. So that's a little historical note there. I think [inaudible] the same way. Yeah. How did that work, and could we do something like that in some way?

*Dr. Elizabeth Unger:* Vicky, are you going to, you want to comment on that?

*Dr. Vicky Whittemore:* Yeah, but I don't want to step on Mary, if Mary got a comment first. Her hand's been up for a while.

*Mary Dimmock:* Oh, I can comment, because mine's on a different topic.

*Dr. Vicky Whittemore:* Okay. Segue. So, I was just going to comment that there's a lot we can learn from the rare disease community. I, as many of you know, I worked for more than 20 years in a small nonprofit for the Tuberous Sclerosis Alliance. There are 50,000 patients estimated in the United States. And there are now 30 centers of excellence, clinical care centers, across the United States. And we started just by having a few, starting with a key physician, most of the time a pediatric neurologist, and then identified the other specialists at that center that those patients needed. So, they needed nephrologists, cardiologists, dermatologists, you name it, G.I. And we just identified, worked with that one clinician to find those people to develop a clinic. And they function within those centers with no funding from anyone.

And so, I think there's a lot that can be learned from how rare disease communities have been able to do this, to put in place these multidisciplinary clinics where a patient comes in and you say, you see the primary physician, but then you say, okay, I also need the dermatologist, and there's coordinated care. And this has been adopted, not only for Tuberous Sclerosis now, but for many of the rare diseases.

So, I think that there's just a lot of ways that we can approach this. And I fully endorse putting together a working group where we can sit down and put our heads together and say how can we do this and make a difference? The other comment I would make is just thinking about early career development and these K awards. Building on the back of what the Open Medicine Foundation has put in place at Stanford, at Mass General, where there are not multiple physicians now involved in the research, who also see patients, and they could be pulling in young investigators to be working with them to do research to build a pipeline. And so just really being creative about how we can think about building the pipeline. But also in terms, I think we can't just build the pipeline, we have to think about how can we provide care today for those who need it. I think it's two pronged. But it's really going to take, as I said, a community and all of us coming together to think about creative ways to do this.

*Dr. Elizabeth Unger:* Okay. Mary.

*Mary Dimmock:* Thanks. Building on what Vicky said, I think it's a good idea to learn from a number of the initiatives that we've discussed today. And as we're doing that, to also look a whether any of those initiatives face some of the barriers that we talked about here, like reimbursement being a big one. So, for instance, in tuberous sclerosis, they were able to set up those centers with no funding because they were actually able to get reimbursement through the insurance systems.

I think we can also, we also might want to look at what the school nurses have been able to do to engage and communicate out to their members and can we learn anything from that that can be used in some of the medical associations that we need to reach? And then finally, we haven't talked about it today, but I think it'll be really important to look at the state health departments and the state health commissioners and what role they can play. In New York State, Dr. Howard Zucker sent a letter out to all the practitioners and clinicians, 85,000 doctors, if I remember correctly, encouraging them to look at ME/CFS and their differential diagnosis. I think we're going to need to think about multi-pronged communication out to these doctors from leaders and associations and institutes like that, that could help drive the change that we need.

*Dr. Elizabeth Unger:* Yeah. Thank you. Related to that, we needed to be sustained, not just a once and done thing.

*Mary Dimmock:* Absolutely.

*Dr. Elizabeth Unger:* We need to figure out ways to continually get the message out in different ways and working together. So, I, we do want to get to a discussion of the systematic review and the clinical trial plans that Vicky had. So, I do, and Vicky agrees that a committee might be a good way to move forward. And so maybe that's what we should try. Vicky did you have another comment? Oh, okay.

Okay so, and I, these questions and comments that we generated I think will be a good starting point for that subcommittee. So, the topic of the systematic review, I've asked Dr. Nanda Issa from our group to give you an overview of where we're at. [Inaudible]. Yes, so if.

*Dr. Nanda Issa:* Okay. Great. Can you hear me this time?

*Dr. Elizabeth Unger:* If we could bring up Nanda's slides.

*Dr. Nanda Issa:* [Slide shows title page] Okay. Great. Thank you, I'll let you know just by saying next slide, Monica. Thank you. So good afternoon. Thank you all for attending this workgroup. My name is Nanda Issa, and as mentioned before, I'm the medical officer here on the team at CDC. And I'll be going over the systematic review of ME/CFS treatment that was conducted by Oregon State, or sorry, Oregon Health and Science University Evidence Based Practice Center, which I'll refer to as OHSU, due to a contract with us.

So, one of the main goals of our ME/CFS program is to educate healthcare providers about ME/CFS, to enable timely detection, diagnosis, and management of the illness, ultimately resulting in improved care for patients and reduced morbidity. And you might recall, from the 2015 IRM report that there was excellent guidance in clinical diagnosis, but it didn't necessarily address the management and treatment of ME/CFS. So, with the ultimate objective of ME/CFS treatment guidelines in mind, we set out to evaluate recent evidence related to treatment of ME/CFS and management of its symptoms. The idea is that once this is developed, the dissemination of ME/CFS treatment guidelines will help equip clinicians to care for patients with ME/CFS using evidence-based recommendations. Next slide.

[Slide shows current review key points in bullet form] Okay, so the current review conducted by OHSU is an update of a review that was previously funded by the agency for healthcare research in [inaudible] AHRQ. The AHRQ report concluded that more studies were needed to fill gaps in ME/CFS research. And the current review differs from the prior review by evaluating evidence for therapeutic intervention effectiveness in children, in addition to adults, and by considering therapeutic interventions targeting symptoms prominently present in ME/CFS.

As case definitions for ME/CFS have evolved and some older definitions, in some cases, have misclassified patients, this report stratifies findings by the definition used for

ME/CFS. Finally, it assesses harms and benefits of diagnosis and treatments. Next slide.

[Slide shows image of people working on a puzzle and lists stakeholder talking points in bullet form] So we recognize that stakeholder engagement in the early part of the systematic review was critical. So, we involved stakeholders as key informants in developing key questions to guide review. These stakeholders included ME/CFS clinical and research experts, individuals representing patient's perspectives, and individuals with family members with ME/CFS. Next slide.

[Slide shows key questions in bullet form] The key questions that the informant developed were as follows. In patients undergoing evaluation for possible ME/CFS, what is the frequency of non-ME/CFS conditions, also referred to as comorbidities? What are the benefits and the harms to the patient of diagnosing ME/CFS versus non diagnosis? What are the benefits and harms of therapeutic interventions for patients with ME/CFS, and how do they vary by patient subgroups? And subgroups were defined by many things, so defined by age, sex, race and ethnicity, presence of bio markers, ME/CFS severity or duration, type of onset, the criteria used to diagnose ME/CFS, and associated comorbidities. These therapeutic interventions targeted symptoms prominently present in people with ME/CFS, such as coarsely, orthostatic intolerance, pain, fatigue, cognitive problems, depression, multiple chemical sensitivity, gastrointestinal symptoms and urinary symptoms. Next slide.

[Slide shows status information in bullet form] The current systematic review completed by OHSU's searched publications through January 2019. Data sources included Ovid MEDLINE, The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, [Inaudible]. The draft report has been cleared by CDC. And to collect comments, we plan to use a federal registry notice, which is going through a separate clearance process. The final report will incorporate the comments from the public through the federal registry notice, and from a peer review conducted by OHSU. And new studies that are identified from an updated search in 2020 will be incorporated in the final report. Next slide.

[Slide shows bottom line findings in bullet form] The bottom line of the current systematic review was that since the last review there have been essentially no therapeutic advances in ME/CFS, as there was very little information on the treatment and management. The new information was limited to the following two major conclusions. There was such limited evidence on medications that the reviewers could not draw conclusions. And there was limited evidence on exercise versus other active therapies. The studies did indicate that exercise probably has a positive effect on the fatigue in adults compared to usual care of passive therapies. However, no evidence to support the applicability of this finding to patients diagnosed with case definitions other than thoughts or [inaudible] criteria was identified in the literature review. The final take home message is that more clinical trials are needed to provide an evidence based for treatment of ME/CFS. Next slide.

[Slide shows next steps in bullet form] As far as next steps go, our team will initiate public comment phase through the federal register notice, as mentioned before. And after finalizing the report, and posting it, along with its comments on our website, we will revisit plans for the treatment guideline development. The CFS Advisory Committee, or CFSAC, was considered a federal advisory committee, or FACA option for this treatment guideline development. But in September 2018, CFSAC was dissolved, and after that we were unable to identify another FACA option. But we did consult with many experts in the agency, and we learned that a non FACA route was the most viable option. We have considered organizing a guideline working group, which would comprise federal experts from multiple disciplines involved in the development of clinical guidelines, from patient representatives to clinicians, methodologists, to name a few.

It's important to note that using these options means the guideline working group has to be made of only federal employees who could elicit outside opinions not only through an FRN but also through an open workshop forum. After the working group develops this guideline draft, another federal notice, register notice could be posted to solicit comments. But given the current situation and the conclusions from the most recent systematic review, perhaps it's not quite the right time to start developing federal clinical

guidelines for ME/CFS. In our consultations with experts, other alternatives, like compiling expert opinion, have been discussed. Next slide.

[Slide lists guidelines in bullet point form] And on that note, it's worth pausing to consider that the landscape has changed since we started this process. There have been a number of clinical guidelines and recommendations put together by experts since this systematic review's process was started. And it's important note that in the absence of systematically collected evidence, these guidelines and recommendations are based solely on expert opinion. These include a primer published in Frontiers in Pediatrics on ME/CFS diagnosis and management, a handout for clinicians on the basics of diagnosis and treatment put together by the U.S. ME/CFS Clinician Coalition, and updated guidelines from the U.K.'s National Institute on Health and Care Excellence, expected to be available this April. Next slide.

So, thank you for your attention, and we look forward to the discussion. Thanks.

*Dr. Elizabeth Unger:* Thank you. And so, we, we felt like this was really impetus to talk about the situation with clinical trials and discussing the situation with Vicky. She thought it was timely to discuss the, her thoughts, and NIH's thoughts on clinical trial design and workshops. So, Vicky.

*Dr. Vicky Whittemore:* Yeah. Thank you. If you can take the slide down, I don't have slides. So more than a year ago, the trans NIH ME/CFS working group discussed organizing a workshop to bring together people to talk about the barriers and challenges to doing clinical trials on ME/CFS, and what could be done to change that landscape. Then COVID hit. And so, our attention was diverted to lots of other things, especially long, or COVID and now long COVID. Excuse me. But the workshop is back on the table, and I think very timely. In terms of thinking about how do we go about putting clinical trials for ME/CFS in place?

And back a year ago, we had a call, we are meaning a few of us from the working group, had a call with representatives from the FDA who were going to be very involved in the workshop, and we would make sure that they were involved again. Because several of the things they pointed out was, number 1, we don't have a bio marker that

can clearly identify and diagnose individuals with ME/CFS. Secondly, we don't have objective measures to look at progress of disease and response to treatment. So as many of you know, Ampligen, there was significant improvement on the clinical outcome that they utilized for that clinical trial, but the FDA felt that it was not clinically significant to the patients. And that the Ampligen, at that time, was not approved by the FDA, as a treatment for ME/CFS. So, our FDA colleagues pointed out that we really have to have objective clinical measures going into clinical trials and know what those are going to be. Along with then, the last part of this, well identified cohorts and the ability to characterize and phenotype the cohorts that are going into these clinical trials such that we have individuals with clear diagnosis. We don't have a mixed bag of individuals who may or may not have ME/CFS. So again, clear clinical, a clear way to diagnose.

And so, we had, at the time, also had, a year ago, several conversations with the people in, Professor Fluge and his colleagues in Norway who have conducted clinical trials for ME/CFS, to learn from them. And they essentially told us exactly the same thing, that they would not go into another clinical trial without having clear bio markers, without having clear objective measurements of response to treatment. So, our, what we feel is needed is to bring people together at this point and say, if these are the things that are needed in order to go into clinical trials, how do we get there, first of all. And once we have those things, how do we identify, as Nancy was suggesting, a clinical trial network who would carry out these clinical trials?

And then I guess, the last piece of it, that I think is maybe more challenging, but I think equally as important, is to understand how we pull industry and pharma into this, as well, so that they're a partner at the table, and thinking this through with us, and trying to understand what are the clinical trials that we could move forward. We, as some of you may know, NINDS supports some clinical trial networks. But for most of those, right, I shouldn't say all, there's one called NeuroNEXT that will do clinical trials on neurological diseases. There's Strokenet, which is specific to stroke. But in all of those situations where there are clinical trial networks, there's a clear pipeline of pre-clinical to translational to clinical research that's feeding into those clinical trial networks. And so it, as the trans NIH working group has discussed it, it's premature to set up a clinical trial

network without having a pipeline of trials coming in, otherwise you're just wasting funding on infrastructure waiting for a clinical trial to come along.

But these are all of the kinds of issues that we really agree need to be addressed. We absolutely agree there needs to be clinical trials done in ME/CFS. But again, it's going to take us coming together and really addressing head on what these issues are and how we can overcome them, whether it's research to develop objective measures. There's a lot of research going on in the funded collaborative centers trying to understand the path of physiology that could lead to those bio markers, as well as in other funded research from the NIH, from OMF, from research that's going on in Europe.

So, bringing all that together to try to understand what it is we need to put in place so that we can go forward with clinical trials. Because clinical trials are incredibly expensive. And to move into clinical trials with just some hope that something is going to work is not going to happen. NIH tends, and looking at Dr. Koroshetz, I may or should not say this, but I think going into clinical trials we're risk adverse. We really want to see that there's strong evidence that this clinical trial is going to be successful, because you're investing a lot of time, a lot of money, a lot of resources into large studies.

So, stay tuned. I'm sure I'll be in touch with many of you about thinking through how to pull this workshop together, because it was timely a year ago, it's even more timely now. And again, there may be aspects of this that we can piggyback on clinical trials that will be coming through for the long COVID. But I think that it's something that we absolutely need to move on, and there's significant interest in doing so. And I would love to hear thoughts from anyone else about this. But I'm just wanting to put out, sort of, our position at NIH. And the recognition that we know this needs to move forward, and we just need to do it in the right way that we can really move into clinical trials in a smart and efficient way that will benefit the community. I see Oved has his hand up.

*Dr. Elizabeth Unger:* Yes, yeah, go for it.

*Oved Amitay:* Thank you, Vicky, this was incredibly encouraging. And we would wholeheartedly support this effort. I can only say from my own experience of 25 years of

developing therapies, mostly in the rare genetic disease space, is that this, you know, this challenge is one of that we face very often with fully understood diseases. I would say one thing, which may surprise you, but industries actually even more risk adverse than NIH. So, this is, you know, this is a familiar situation.

The only way to address it would be for, ultimately for the FDA to issue what they often do, which is a white paper guidance to the industry, in which they describe what is acceptable, what is not acceptable, and what is negotiable. And that gives the industry a sense of what's on the table. In other words, what are the end points would appear, patient report outcome, a measurement of quality of life for instance, is that something that would be acceptable. I think it would have to apply, the FDA would need to apply the risk management calculation that they do for rare diseases, [inaudible] diseases. Although epidemiologically, ME/CFS is not one, I think it really deserves to be treated as such.

And so, if there's anything that we can do to support this kind of a workshop from the patient community, we're in. And I think you're right. This is something that needs to happen, and which is why we definitely need to have the FDA be part of this discussion.

*Dr. Vicky Whittemore:* Absolutely. The FDA did issue a white paper. I'm not remembering when. Beth may remember when, but many years ago. But absolutely. We do need to engage them in this discussion, right? Absolutely.

*Dr. Elizabeth Unger:* Yeah. They have an initiative to qualify markers for end points in clinical trials. And the PROMIS instrument is PROMIS fatigue, is being advanced as one. It's almost, we've been collaborating with a group that's trying to get it fully qualified as an endpoint. And you know, the work is slow, and but it's progressing. So, but I, so I think it's timely to totally revisit this. It has been a number of years. So, Dr. Argue, do you have a comment?

*Dr. Kathryn Argue:* Yes. I just wanted to mention a few of the ways that CDMRP can kind of help with this de-risking clinical trials. We do kind of have some ways in which we can be helped with this. One is that we do offer an award mechanism that does not really require preliminary data. It's a discovery award. This is also something that can be

applied to for anyone at the postdoctoral level or above, so it helps with kind of that workforce development problem with getting young investigators in. But if there is a new idea, they can start there. And it has a direct pipeline into being able to progress into a clinical trial with an expansion funding option.

The other thing is that we do offer an award mechanism called a therapeutic development award that offers funding for some of these more boring aspects of getting therapy through to the FDA, such as funding applying for an IND, and just kind of completing some of the pharmacological and toxicology work that you need to do that when you have a potential drug candidate.

And then lastly, we are able to fund for profit organizations. So, if there is a pharmaceutical partner that is interested, or has a candidate, we can offer funding for them to help relieve some of the risk from a for profit company in order to help. And that's kind of, you know, where we help out with rare diseases, is to de-risk this for both non-profit and for-profit partners. So, I'm happy to answer more questions, if anyone wants to know more about those opportunities.

*Dr. Elizabeth Unger:* Thank you. And Mary?

*Mary Dimmock:* It's really great to hear about the opportunities that Dr. Argue just talked about. That could be potentially very useful. I also wanted to go back to what Vicky said about the pre-clinical to clinical pipeline that needs to be in place. I spent enough time in the pharma industry to understand how important that is. But in this case, we don't have that.

But what we do have are therapies that are being used off label successfully to help treat the symptoms of this disease. And it seems like we should be able to take advantage of those therapies, and run clinical trials on those therapies, to better learn how to assess the improvement that patients are seeing. How do you characterize it? How do you measure it? What do you have to do initially? And with follow up to really understand that I understand the complexity of doing that, and the disease, where there is the kind of fluctuation that we see here. But I think we could learn a lot from it.

I think the other thing that would be really beneficial in those is that they could be designed in a way where you could actually learn something about the mechanism that would then feed back into pre-clinical work as they're trying to sort through the basic mechanisms of the disease that need to be, that need be understood. Thank you.

*Dr. Vicky Whittemore:* Absolutely. And I don't, at all, disagree with you Mary. And as you know, NIH supports investigator initiative awards, and we have said multiple times that investigators should come to us and talk to us about their ideas for clinical trials. We are not going to send out checks. We use the peer review system. And so, we're open to discussions. And they just, we have, they haven't happened.

So, we need investigators to come forward and say, these trials need to be done, let's think about how we could put this in place. You know, we're not going to tell investigators what to do. They need to come to us and tell us that they have these ideas, help us design this, how do we think through how this could get through the peer review system and be a funded clinical trial.

*Mary Dimmock:* Right. I totally understand what you're saying. I think that starting to establish that clinical trials network might help provide some of the support for making that happen. It's kind of a chicken and an egg situation.

*Dr. Vicky Whittemore:* Sure. Absolutely. You need the clinical trial, so people, in place to think through putting the clinical trial in place. Absolutely.

*Mary Dimmock:* Exactly.

*Dr. Elizabeth Unger:* So, can I kind of go backwards to the discussion about the treatment guidelines. And are, you know, we'd like some of the other group, other panelists to comment on our suggestion that perhaps now is not the right time to pursue clinical treatment guidelines at the federal level, given the difficulties of having only federal employees on the committee and indirect transmission of information, and that it would be at the level of expert opinion, which is expert opinion guidelines are available. Yes.

*Ben HsuBorger:* Dr. Unger this is Ben HsuBorger with ME Action. I think from ME Action's position, talking to many people, both working in the U.S. and the U.K, and other places, would recommend those, that would be our position, I believe, that you know, we don't want to simply recycle the old evidence base. We all know the problems with the pace trial, these other things, and you know, I think our core reservations were about, from the previous evidence review that was done, when it was revised that was, you know, submitted in a peer review journal where it was accessed. And it would be, you know, very, one of my core concerns is whatever, if something was to come out that resets, restates the previous flawed evidence base, if it would [inaudible] the stigma, the harm. And I know, you know, we're talking about like scientific processes and collecting knowledge and evidence bases, but also you know, the practical real-world interpretation that if people don't see a clear reputation and understand the flaws in the previous evidence base, so that could do more harm than good.

So, I would, those reservations about moving forward at this time before doing more to work to increase the evidence base, and you know these are things that we have been communicating for the past couple of years. But looking to the clinician experts, or clinician researcher experts that we do have for guidance what we can know well about this disease and treatment.

*Dr. Elizabeth Unger:* Thank you. Oved. You're on mute.

*Oved Amitay:* Sorry, I actually was lowering my hand. Nothing.

*Dr. Elizabeth Unger:* Oh, lower your hand. Okay. Mary are you a lower your hand, too?

*Mary Dimmock:* No. I just want to add to what Ben said. But also, reflecting on the comments that came in from the clinician's survey. It was really, really strongly reinforced. The trouble that they're having getting uptake is that the practices that they have don't match what's in the evidence base. We lack the evidence base. So, trying to build on a systematic review, and then having only federal employees involved, I think it would be much better to look at what other options we have, as you point out, given the changing circumstances.

*Dr. Elizabeth Unger:* Okay. All right. Yes.

*Ben HsuBorger:* Can I ask one question, Dr. Unger?

*Dr. Elizabeth Unger:* Yes.

*Dr. Ben Hsu Borger:* Is there, hearing about a workshop for clinical trials is good, it is exciting news. I'm glad we're at that point of having that discussion. You know? And we want to be at the point place of like pursuing a bio marker. Given all these, you know, challenges we're facing now, is there a, where we at in terms of clarifying, is there interim work we can do to clarify the instrumentation that we use for selecting patients for clinical trials for this research.

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* That's, that you know, for patient recruitment selection methods.

*Dr. Elizabeth Unger:* Yes.

*Ben HsuBorger:* Can we use some of the knowledge that exists in the expert guideline to get some uniformity so that those who may be coming new into this are all using, kind of, our best knowledge at the time, of how to.

*Dr. Elizabeth Unger:* Yeah, that's a really good point. And that was really the hope of our, at least partly, the common data elements project that CDC and NIH did together. We've gotten to a certain point with that. I think what's missing is we've got the measurement; we don't have the thresholds. In other words, to meet any particular criteria we don't have any recommendations on what those thresholds would be.

However, I feel like the data should be available as people start, as you know, they can use these instruments and we can start trying to establish what is the, what is the best threshold for whichever measurement we're doing to say that a symptom is present. And you know, CDC has some preliminary data on those, and what thresholds we have used. And but, you know, definitely more work needs to be done.

But I think the key is we need to move away from thinking ME/CFS is one thing, and a clinical trial of ME/CFS is not going to work. You're going to need a particular kind of ME/CFS to target to do this phenotyping so that you are looking at either people that are early onset with XY and Z or you know, some combination. I don't have the answers,

but I know that ME/CFS as an entity is not feasible. That's my belief. There's no, that's just my belief. Sorry. So, Charmian.

*Dr. Walter Oroshetz:* That's true about a lot of diseases, too.

*Dr. Elizabeth Unger:* Yeah.

*Dr. Walter Oroshetz:* I mean, even Alzheimer's.

*Dr. Elizabeth Unger:* Yes. Not one thing.

*Dr. Walter Oroshetz:* It's not clear, you just can't take all of it. Good point, too, trying to go after, trying to understand what measures would be useful in clinical trials and how they perform before you go into the trial is absolutely necessary. That's the kind of research that we would certainly fund.

*Charmian Prokskauer:* I was also going to make that same point. And there's such a difference in the clustering of symptoms among people with ME/CFS, and maybe it would be almost a good idea to look at, I don't know, I shouldn't be suggesting this, I'm not a doctor, but one symptom at a time, or one system at a time. Things that are going on elsewhere in the body may also be influencing that.

It's just very, it's a very complex, its presentation, and there are many different phenotypes. It's hard to, I think a lot of times that we get sort of you know, no real results is because we're throwing a whole lot of different things into the same pot, and then nothing stands out.

*Dr. Elizabeth Unger:* And one other point that I just, I'm always amazed at how many medications some patients are taking, and how that has to complicate the measurements that we're doing, and the response to other therapies. And you know, it's difficult in the patients with long standing illness, which is why I think moving our consideration up into the early phase of illness is an important consideration. Not that we shouldn't look at long phase illness as well, but we may get some different insights if we start earlier on in illness. We are getting towards the end, so Mary did you have another comment?

*Mary Dimmock:* Yeah, just really quickly. I get your point about enrichment clinical trials to make sure you get a clear signal coming through. I think that it would be worth a formal effort with the clinicians, some knowledge retention effort if you will, or knowledge gathering effort, to understand how they make the decisions when they are deciding that this patient needs a particular medication and that patient needs another, because I think that could help with enrichment strategies, by understanding how they phenotype, make those phenotyping decisions and their treatment decisions.

*Dr. Elizabeth Unger:* Yeah. We had tried a little project many years ago called, you know, trying to capture clinician intuition, we were calling it. You know, what sort of thought process clinicians go through to take care of their patients. And it was very complex. It was a great idea, but it was difficult to actually get something concrete out of it, but we just.

*Mary Dimmock:* I think it may be worth trying it again.

*Dr. Elizabeth Unger:* Yeah. Yeah. So, any closing comments, anybody from CDC? Dr. Damon?

*Dr. Inger Damon:* So sure. So really, thanks everybody for a great discussion, and really sharing ideas and thoughts. You know, also using the Q and A functions in chat to engage others in the discussion. I think we heard some exciting new developments over the course of today, in terms of thinking about training and education and workforce, some of the clinical trials work that's thinking about moving forward in terms of the workshop. And so, I look forward to tomorrow's discussion where we focus more on long COVID and updates to this community on research activities and cross agency collaborations.

*Dr. Elizabeth Unger:* Okay.

*Dr. Walter Koroshetz:* Can I just add that from my standpoint, I really appreciate the folks coming together and think we can all, we all honestly see the magnitude of the problem. I don't think anybody, you know, is blind to that. And so, it's only working together that we're going to get there. But we're not going to give up. Nobody on this call is giving up. So just got to keep pushing forward and, you know, do it together. I

think that's, I mean, that's the really good thing about this meeting is to see how everybody has different opinions but we're all trying to get to the same place. Very uplifting. Thank you.

*Dr. Elizabeth Unger:* Okay. Thank you. Thank everybody. It's like.

*Dr. Inger Damon:* I have, like we have a last comment from.

*Dr. Elizabeth Unger:* Oh, Charmian, last comment?

*Charmian Prokskauer:* I just wanted to thank the people who've been writing in the chat, and the Q and A. We've heard a lot of, we see a lot of patient voices in there, as well. And some perspectives that we didn't capture in our presentation. I think all of the input from people who are living with these diseases is really important, and I hope people will pay attention to those.

*Dr. Elizabeth Unger:* Yes. Thank you. Is there any one last question, because we have 4 minutes. Christine, was there anyone, one? You're on mute.

*Christine Pearson:* Sorry about that. There are a lot.

*Dr. Elizabeth Unger:* Yes. Okay.

*Christine Pearson:* But I think a lot of them, it looks like some of our panelists have also been answering. So let me.

*Dr. Vicky Whittemore:* From the NIH, I'll just say that we would be happy to answer the questions that were in the chat. I saw that some of them were not directly related to the conversation today. But we would be happy to address those questions after the meeting.

*Dr. Elizabeth Unger:* Okay, so we'll work on compiling some of them.

*Christine Pearson:* Actually, that's a good question. Monica is there a way to save all of them that are in the chat, in the questions as we're going along, or before?

*Monica Payne:* Yes, I actually just pinged Courtney and said after the meeting I will send you all reports, Q and A chats, and everything else.

*Christine Pearson:* Excellent. I should have thought to ask that earlier. Appreciate it.

*Monica Payne:* No problem.

*Dr. Elizabeth Unger:* Okay. Well, thank you, everybody. I think it's been a great day, or I mean a great afternoon. Just and we will begin again tomorrow afternoon. Thank you.

*Dr. Inger Damon:* Thanks.

*Dr. Vicky Whittemore:* Thank you everyone.

*Dr. Inger Damon:* Thanks Beth and Vicky, on your work on getting this agenda together.

*Dr. Vicky Whittemore:* Thank you. Goodnight.