NIH ME/CFS Advocacy Call
March 4, 2024

Barbara McMakin: Good morning, everyone. My name is Barbara McMakin and I'm from the NINDS Office of Neuroscience Communications and Engagement. On behalf of the NIH, I'd like to welcome you to today's call and thank you for your interest in participating in this discussion with us today. Today's call is being recorded. If you have any objections, please disconnect at this time.

During today's webinar, we will be discussing the ME/CFS Research Roadmap, which is currently being developed. Today you will hear from Drs. Vicky Whittemore, Maureen Hanson, and Cindy Bateman, who will give an overview of the Research Roadmap process, describe the goals of the roadmap, discuss the research priorities, as well as next steps.

After their presentations, we will open up the call for your questions and comments about the research roadmap. Because our time is limited, today we kindly request that questions and comments be about the roadmap. If you have questions or comments about other ME/CFS research and activities, please e-mail us and we will reply as soon as we can. I will post the e-mail address in the chat. We are unable to answer questions about your personal medical situation or offer medical advice, so please refrain from providing any personal medical information this morning.

I would also like to mention that we are working to schedule another webinar which will follow our usual format. As soon as we have the date and Zoom details available for that call, we will share the information with the ME/CFS listserv. So please keep an eye out for that announcement. During today's Q and A session, if you have a question for our speakers, please select the raise hand button at the bottom of your Zoom screen and we will call on you to unmute. If you are joining us by phone, please dial *9 to raise or lower your hand and *6 to mute and unmute. You can also submit questions using the Zoom Q and A box. We will try to answer as many questions as possible in the time we have available to us today. Now I would like to hand the call over to Dr. Vicky Whittemore.

Dr. Vicky Whittemore: Thank you, Barbara. And let me start by sharing my screen here. All right. So thank you everyone for joining us today. And it's my pleasure to welcome Drs. Bateman and Hanson to join me in this presentation. But I'll start by giving you some background information about the process and then turn it over to Cindy and then followed by Maureen.

So first of all, as I think many of you know, NIH coordinates research on ME/CFS through the Trans-NIH ME/CFS Working Group that's chaired by Dr. Koroshetz, the director of NINDS. And we have program directors from across many NIH Institutes and Centers at NIH that carry out this work. So the program directors who are part of this Working Group are from what we call our extramural program, which is the program I'm part of at NINDS. And these are the

programs that provide research funding and training funding that's carried out outside of NIH, so across academic institutions across the United States and in some foreign countries. The intramural program is the research and training that takes place at NIH facilities, so NIH laboratories in Bethesda or at other locations in the United States. So our focus of the Trans-NIH ME/CFS Working Group is on coordination of research across NIH.

So in 2019, there was a report to the National Institute of Neurological Disorders and Stroke Advisory Council that recommended one of the recommendations that came from that was that NIH should initiate a strategic planning process for research on ME/CFS. And the report can be found on the NIH NINDS website or on the ME/CFS website which is also on the NIH website.

So we initiated a planning process and we had planned to start this initiative when the pandemic broke out and it was became very clear that the clinicians and investigators just did not have the time or ability to focus. And we at NIH also didn't have the ability to focus on the effort during the early phases of the pandemic. So we restarted the process in the fall of 2022 and actually launched the actual development of the research roadmap in February of 2023. So we've been at this now for more than a year.

The process we've used to establish the Working Group of Council and identify people with lived experience is that we put out a solicitation to invite individuals with lived experience. So these are individuals who themselves have ME/CFS or their caregivers or family members to either be nominated or self-nominate to participate in the process. And from that, we received over, I think about 92 nominations and 21 individuals were invited to participate in this process. They joined the individuals who were appointed to the Working Group of Council that includes individuals who are healthcare providers, researchers, clinicians, scientists, leaders of the patient advocacy groups, as well as additional individuals with lived experience. So all of these individuals then were divided into eight webinar planning groups.

The charge to this Working Group of Council and the people with lived experience is to develop a research roadmap to provide scientific guidance to the Council on how to best advance research on ME/CFS. So consistent with the charge, the group will assess current ME/CFS research activities and identify opportunities and gaps in ME/CFS research to identify targets for the development of treatments.

So a lot of the discussions and as we went through the webinars was really to focus on what do we need to know, what do we know, what do we need to know to really accelerate the research toward the development of treatments for ME/CFS. So this is a list of the individuals that are serving on the Working Group of Council, co-Chaired by Cindy Bateman and Maureen Hanson, and includes the individuals with lived experience who joined us in this effort. And we put out a huge thanks to all of these individuals who have spent a tremendous amount of time helping us with this process.

So the domains for the eight webinars that we put in place were nervous system, immune system, metabolism, genetics, chronic infections, physiology, less studied pathologies, and circulation. And from these webinars, each of the groups developed a set of research priorities. And those research priorities have been posted on IdeaScale for community feedback. So as of this morning, we've had 222 ideas submitted and an additional 101 comments to those ideas and they keep coming in. I keep seeing them coming in on my e-mail and those comments will be open, IdeaScale will be open until March 8th, and I'll come back to how you can comment through IdeaScale or by e-mail as well.

So I just wanted to identify who was on all of these webinar planning groups. And you can see that they were chaired by individuals on the Working Group of Council and then included individuals from the Working Group of Council and people with lived experience.

So the timeline, as I said for this actual process, this was at the webinars, were held between August of 2023 and January of 2024. We've just received the last of the draft reports. Well, the research priorities were developed and posted on IdeaScale. We've just received the last of the reports and are in the process now of pulling all eight of the reports from the webinars together into an overall report that will be completed and sent back out to the Working Group of Council and the people with lived experience for review and feedback. Also taking into account all of the feedback that we've received through e-mail and on IdeaScale in April, the final report will be sent to NINDS leadership and to the NINDS Advisory Council and the report will be presented publicly during the open session of Council on May 15th and more information will be sent out about how to join that meeting in the near future.

So for more information about the ME/CFS Research Roadmap, you can find that on the NIH website. If you go to the website and just type in ME/CFS Working Group of Council, it will take you to this information and the video recordings and transcripts from all eight of the webinars have been posted on this website. Again, you can reach that through the information on the NINDS website as well as ways to provide feedback. As I said, you can go to IdeaScale and provide this feedback or you can send an e-mail to MECFSresearchroadmap@ninds.nih.gov and we will post that your feedback onto IdeaScale for you. And the best way to receive announcements and updates as we go forward is to sign up for the listserv by going to this link and signing up for that listserv.

And I just would like to really give a huge shout out to our NIH team who have really helped behind the scenes on to really help with all the logistics coordination of all of these eight working groups and webinars and this process as we've gone forward. And we also couldn't have done this without our contractors from RLA, especially Holly Riley, Damon Kane, and the science writers that helped us to take notes throughout the process. So with that, I'm going to turn it over to Dr. Bateman for her comments. Cindy?

Dr. Cindy Bateman: Thank you very much. Vicky, I appreciate what you've shared already. I just want to take a few minutes and share a little bit about my experience and a little bit more background information for everyone. Next slide.

This was a really challenging and complex process. I think sometimes it's hard to appreciate. I wanted to start out by thanking the NIH and RLA teams for providing that labor intensive leadership and infrastructure to make it possible for us. And yeah, I'm sure that it ended up being a lot more at work than they thought it might be. That's always the case with big projects. This challenging and complex project required hundreds of hours and was carried out by volunteers. I think we need to appreciate that across the spectrum of ME/CFS, stakeholders, people who volunteered their time and a lot of it, scientists, clinicians, advocates and highly qualified people with lived experience who really paid a high price for their participation.

And it has taken a year for all the logistics, identifying, inviting, coordinating schedules, reviewing literature, preparing lectures and implementing these webinars. Not to mention trying to figure out what to do with all the information. It is challenging to address a complex multi-system disease in manageable but overlapping topics and subtopics.

We talked a long time about how to make this a manageable approach in such a complex situation. And it's going to, and it is taking, and will take us some time to distill the hours of webinar lectures and research priorities. I also wanted to mention that there are originally seven webinar topics, but the Working Group realized that some important emerging topics were missing. So the 8th webinar was added called the Lesser Study Pathologies. Next slide.

So why was this project important? Just some additional thoughts. Of course, it was to carry out our mission to assess current research activities and get this information to the NINDS Council. But there are also some really important reasons why this project was important. One is to create an updated summary of an explosion of scientific progress since the IOM Evidence Review that was published in 2015, and also to focus specifically on ME/CFS while still recognizing the new knowledge we may gain from studying Long COVID. We tried to keep the focus on ME/CFS and to provide a forum for the participants to consider the many dimensions of this complex multi-system disease and emerge from our silos, so to speak, but to foster creativity and create collaborations. Because we're never going to move forward with this disease if we stay in our silos, we've got to understand how all these arenas interact with each other. And also it was important to immortalize the combined expertise and make it publicly and widely available. And you know, you can just YouTube the ME/CFS Research Roadmap webinars and go to all those webinars and you can enjoy them at your own pace. Next slide, I thought it might be interesting for you to see if, for people who weren't able to attend the webinars, these were the agendas. And each of these topics, were one or two or three speakers underneath the eight webinars. And you can see that there's just a lot of depth and detail to the things that we all tried to teach each other in these webinars. Next slide.

And I also as someone who's kind of been around a long time and I was also on the IOM Committee that wrote that report, I put in red and I just did this as a gestalt, but I put in red things that are kind of new topics actually. I mean, we made progress in every topic. There's been progress since 2015, but some of them were like brand new topics that we have known very little about. So I'm very, very optimistic and grateful to all the people who came and joined in this effort, gave their time, and I think it's going to provide a legacy of information for our field. Next slide. And now I'd like to turn it over to Maureen Hanson.

Dr. Maureen Hanson: Okay, I'm having a little issue sharing my screen, but I'm going to in a second. Okay, sorry. I see. Sorry about that.

Dr. Vicky Whittemore: You want me to share my screen again, Maureen?

Dr. Maureen Hanson: No, I don't know what's going on here. Let's see. Well, I know what I can do. Okay. So can you see the slides?

Dr. Vicky Whittemore: Yes, we can.

Dr. Maureen Hanson: Okay, good. So what I wanted to bring up is what are some common themes and research priorities for two more of these eight areas. And as Vicky told you, we had these webinars on these eight different topics. So I don't want to go through each one of these individually. But what I did is I went through and found some cross-cutting themes between these and now I'd like to describe some of those cross-cutting themes.

So one of the one of them was that it is really necessary to have sufficient cohort sizes and we need to represent the proper demographics, variety of demographics, and we have to focus on age and sex and the stage of illness and comorbid conditions. We need to consider sex differences and research findings that can necessitate the sex-specific data analysis, and that's certainly been reinforced by some recent work. We need to consider the subtypes of ME/CFS cases when analyzing data. There's plenty of information now suggesting that there are subtypes of ME/CFS.

We also need to implement longitudinal analysis and research when it's feasible to follow subjects over time. And a key example that I'd like to give is before and after induction of post-exertional malaise. Given that is an extremely important symptom of the illness, we need to have an expansion of ME/CFS biorepositories to include a range of tissues as well as biofluids. That was emphasized by a large number of the different groups. We also need to analyze data gathered from different experimental types, different research fields. Like you know, do multi-omics, for example, to increase the precision and accuracy of identifying ME/CFS signatures. And we need to take advantage of the tremendous developments, the statistical methods such as machine learning, as well as artificial intelligence methods that are now making a big difference in a number of scientific fields.

We also need to compare pre-pandemic ME/CFS to those Long COVID cases that fulfill ME/CFS diagnostic criteria. Without doing this, we won't know whether the same pathways are affected in both and we also need to know, however, are there differences that can distinguish these pre-pandemic to post-pandemic ME/CFS cases that fulfill ME/CFS criteria. And another emphasis that was pointed out is that we really need to have more education of healthcare providers and provide them with an objective diagnostic test if possible. But if that's not possible, we still need to educate healthcare providers and how to diagnose the cases.

We've highlighted the fact that there is new knowledge needed to make discoveries that will identify additional drugs for clinical trials. But the other thing that most of the groups found is that we need to initiate clinical trials using repurposed drugs that are based on existing knowledge. I personally believe there are many, many drugs now known that are being suggested by existing knowledge that we should be using to initiate clinical trials. In these clinical trials, it's going to be important to identify the patient subsets who might respond differently in clinical trials than others.

And finally, we need to use a wide range of tools for the evaluation of these clinical trial outcomes. This gets to the point that we may not need an objective marker to know whether a trial or a drug is working, if it's obviously overwhelmingly evident that the participants are improving in their condition. There are even surveys can tell you whether someone is improving.

Finally, I'd like to comment that I've been looking through the comments that are the ideas that have been put onto IdeaScale, but I did not incorporate all of those into this list of overarching themes because the deadline for the submission of the IdeaScale ideas has not occurred yet. So I didn't want to include that yet, but I will say, when I look through there, I can see that we have some excellent citizens, citizen scientists out there. Because a number of the things that people were suggesting are actually underway in some labs and so many of the ideas, I already can say are ones that scientists themselves also researchers in ME/CFS have decided are very important to do. But there are undoubtedly some ideas that nobody is working on. And so I do encourage people to continue to work on submitting ideas to the IdeaScale. So I'm going to stop here and I guess we'll have Q and A now.

Barbara McMakin: Thanks so much, Dr. Hanson, Dr. Bateman, and Dr. Whittemore for those presentations. We will now transition to the Q and A session and open the floor for your questions. If you'd like to ask a question, please use the raise hand button at the bottom of your screen or raise your hand if you're on the phone. You can also submit questions using the Q and A box. If you are joining us by phone, please dial *9 to raise or lower your hand and *6 to mute or unmute. As a reminder, please do not share personal medical information as we cannot provide medical advice on the call today. In addition, we ask that questions be about the ME/CFS Research Roadmap.

So we'll start with some of the questions that we've gotten in the Q and A box. And Dr. Bateman, I will direct these to you. They are both about fibromyalgia. Do you consider fibromyalgia to

have similar etiology as ME/CFS? Should they be included in these studies? If not, what is your reasoning?

And then a similar question. Fibromyalgia also has the same or very similar symptoms as ME/CFS as well as Long COVID. So why isn't fibromyalgia included in these research projects?

Dr. Cindy Bateman: Very good question. As a clinician who's worked across these illnesses for many years, I'll tell you that the way we define these illnesses creates a lot of overlap and so getting a diagnosis in the community is not necessarily a good way to divide. When we diagnose ME/CFS, we acknowledge the presence of pain amplification like is seen in fibromyalgia. We are definitely focusing on the people who have post-exertional malaise and have dramatically impacted function, and there's a lot of people with fibromyalgia who can exercise and improve their situation with fitness and medications.

So I do think we take into account the subset of patients who have a lot of pain that is very similar to fibromyalgia and we'll just kind of have to wait as we get objective biomarkers. I will say that the science of chronic pain and pain amplification is far more advanced than the amount of science we have to understand ME/CFS. So we're trying to focus on the underserved component and those that are more ill. I hope that's helpful.

Barbara McMakin: Thank you. Another question we've received is how will NIH include people over 65 with ME/CFS who are usually excluded from participating in research studies? Dr. Hanson, I don't know if you want to address that?

Dr. Maureen Hanson: We actually included people up to the age of 70 in our studies. One issue of including people over that age is if there is an event, intervention involved, it becomes more problematic. So in our studies, for example, that included a cardiopulmonary exercise test, we couldn't include people over 70 because we wouldn't get approval for that for our human subjects. But for other purposes I see no reason why people over 70 could not be included if for example it's a simple blood draw. And I certainly hope that people over 70 will be included in those studies, it will have to, you know, people over 70 do have issues that have to do with age. So it is going to, you know, require some consideration of those age-related differences. But I see no reason why researchers can't include people over 70, as long as the intervention or the participation in the study is not going to be more harmful for people over 70.

Dr. Cindy Bateman: Can I add something to that? From the clinical standpoint, the huge need is clinical care for people of all ages because sometimes it seems like research is the only avenue to getting a diagnosis right. But if everybody got the care across all the age spectrum then it wouldn't feel so, people wouldn't feel so neglected not joining studies. And since I take care of people across all the age groups, I'll say that the older people get, the more confusing it gets about what's causing their fatigue and their sleep problems because of age-related changes and comorbidities. So that's part of the reason people get excluded, right?

And I think this is a question for all of our speakers, how can we prioritize research into the less studied pathologies for the NIH Research Roadmap? They are important research priorities and need research funding. They include ME/CFS, connective tissue disorders, spinal disorders, mast cell activation syndrome, gastrointestinal conditions, endocrine dysfunction, hormones and reproductive health conditions. I think that was an important part of the roadmap initiative, was adding that that final webinar to really be able to bring these kind of new comorbid conditions that are, we are very actively studying and thinking about in the clinical realm. And just having them as part of this report will be a foundation for amplifying further research, I'm hoping.

Dr. Vicky Whittemore: Yeah, I can respond to that as well. I absolutely agree with that and we have already received some applications on these topics at NIH and we'll continue to encourage individuals to do so. After the roadmap is reviewed and approved by Council, we will really put out a notice that these are the potential research priorities, not excluding things not on the research priorities, but really that these research priorities are and should be the focus for grant applications coming into NIH. So you know, we just will really work with investigators to encourage them to submit those applications for review.

Barbara McMakin: Okay, great. Thank you. Now we're going to hear from some of our attendees that have their hands raised. We'll start with Scott Daniska, you want to unmute, please?

Scott Daniska: Hi, can you hear me? Yes. Hi, thank you for taking my question today. I appreciate your time and the opportunity. And so I had a question about the roadmap. In the timeline that you presented, that there's eight areas of focus that you want to study, being nervous system and chronic infections and so forth. And I noticed that none of those main areas of study are environmental. And I'm wondering why that isn't a main area of study?

We know there's like so many conditions and diseases where the environment plays a large role in the disease. For example, I just read an article the other day about a chemical used at dry cleaners that leads to a 400% increase in Parkinson's. And so, you know, with millions of people affected, I'm surprised that no single doctor or researcher has ever thought like, hey, let's look in people's homes and, you know, see if there's any environmental component to the illness. I've issued a survey myself to a few different chronic fatigue syndrome groups. 80% of patients have self-identified as having multiple chemical sensitivity.

And so I think that if there is an upstream driver, you know, if we're trying to look at causation, you're not going to find that if all of your studies is only downstream symptoms, like if you're looking at the nervous system that's never going to give you answers as to causation and what's driving it. I would think that you'd want that to be a major area of focus. And I didn't see that on your timeline. So I wanted to ask about that. Thank you.

Barbara McMakin: Great. Thank you.

Dr. Vicky Whittemore: Well, thank you, Scott. I think that's really, really an important observation. And we focused I think more on body systems than on potential external causes. But I absolutely take your point and I think it's an excellent point. There are individuals from the National Institute of Environmental Health Sciences on the Trans-NIH Working Group and we've had conversations with them as well as with our ONETOX office at NINDS that's focused on exposures. So I think that's something that we can still add into the report even though it wasn't a focus of any of the webinars. So I appreciate that comment. Thank you. I don't know if Cindy or Maureen want to say anything?

Dr. Cindy Bateman: Yeah, I can add a couple comments and that is I'm hopeful that adding that whole topic of mast cell activation will raise awareness and lead to additional studies of what kind of exposures trigger an immune response or anything that is related to cytokine release, including neurologic symptoms. So I agree with you that it's a big field. It has, you know there's a lot to learn, right? I'll just say that.

Dr. Maureen Hanson: I'd like to comment also that actually there is some work going on in that area, but it's not implicitly mentioned in the roadmap and that is in the metabolism area. When you look at metabolites in you know, in the blood, you can find out about exposures to these environmental chemicals. And so there are actually labs that are doing this. In fact, we have done it and other groups are actually looking specifically. I know of some work in which people are specifically looking into it the in the field called exposomics, looking specifically to see if there's differences in exposures of people with ME/CFS versus people who are healthy. So there is some work going in that area, but I think it could be implicitly mentioned in the roadmap.

Barbara McMakin: Okay, great. Thank you. Next let's hear from Bridget Collins. Bridget, you can unmute.

Bridget Collins: Thank you. I was wondering if the Trans-NIH Working Group has a patient or patient representative as part of it?

Dr. Vicky Whittemore: So no, we do not. And the reason for that is that a lot of the discussions we have are about new research initiatives, new funding opportunities that we can't include individuals from outside NIH in those conversations with because of the indication that it might give someone an early advantage if they have information before other people in the public do. So a lot of the our discussions are very internal to NIH policy and NIH funding opportunities. That's not to say though that we don't regularly have interaction and conversations with individuals with lived experience and many of us have very active ongoing conversations and exchanges with many of the patient advocacy groups as well.

Barbara McMakin: Great, Thank you. Next we'll hear from Peter Cariani. Peter, you can unmute your line.

Peter Cariani: Hi. I was just wondering what it would take to get an NIH disease registry for ME/CFS? I know I saw on the website there were about 30 other diseases that have registries and I think it would be a big boost for researchers and clinicians to have some sort of central clearing house that's sponsored by the NIH. So should that be a part of the current roadmap? That's, that's my question.

Dr. Vicky Whittemore: So typically NIH doesn't support, doesn't well, let me put it this way. So typically NIH supports registries in conjunction with research studies. So there was discussion at the early phases of funding of the ME/CFS Collaborative Centers about establishing a patient registry and we actually partnered with Solve ME/CFS and provided significant funding for the development of their registry. It's something that we can look at and re-address to see if there's a need, but we know that there are other registries out there. But it's something that we can take a look at again Peter, thank you.

Barbara McMakin: Thank you. Next we'll hear from Andrew Lidral. Andrew, you can unmute your line.

Andrew Lidral: So first I'm really grateful for all that you're doing. It's been a journey for me. It's been a struggle and to be working in a field or being affected by something where it's kind of a mysterious disease is really, really difficult and it's impacted my life a lot. So thank you. My question is about medical education. I've been funded by NIH and Abbott. So I understand your mission is more research-based, but one of the biggest things that I've run into is I've probably seen over 20 providers across broad spectrum of specialties over the last five years and I'd say probably 2/3 of them have no understanding of ME/CFS. And the biggest thing I've run into is the gaslighting that happens and being told it's in my head.

So I don't know if it's in the wheelhouse NIH of to do this, but I noticed in the eight domains that medical education wasn't part of that. Is there any possibility for NIH to find avenues to disseminate information, you know, specifically to medical education, whether they're existing providers or in the trainee programs? And I've asked residents that are, you know, following in family medicine, residents that are, you know, following the provider, I'm saying, you know, what are they taught? They're literally telling me nothing. They're not exposed to it. So thank you.

Barbara McMakin: Good question.

Dr. Vicky Whittemore: Typically, that is, medical education is not within the NINDS mission or NIH missions other than we do release press releases and hold webinar conferences to put out

the information that comes from NIH funded research. The CDC, it's really within the CDC's mission to foster medical education. And maybe I'll turn to Cindy because there are some pretty extensive medical education efforts ongoing in the nonprofit area both with MEAction and the Open Medicine Foundation. I don't know Cindy, if you'd like to comment on that?

Dr. Cindy Bateman: Sure, yes, it's one of my favorite topics. There's a vicious circle right, about medical education, because until the research is done and the evidence base exists, it won't be taught in medical school. So we've tried to figure out ways to kind of push both agendas. But the nonprofit I work for, the Bateman Horn Center, has funding. We've been doing medical education. We also have funding from Open Medicine Foundation to partner, and we have spent several years trying to figure out how to get medical education available. But it's a tough one, and it may, it's beyond the scope of this, except to say we have to get key people in academics and in professional societies, and in places that license and provide credentialing, all those places need to buy in. And in order for us to be able to get these kinds of materials in medical schools. Our website has a rich amount of medical education. But you have to come to it. But you, I welcome you to explore it and if you have other questions, you can feel free to contact me.

Dr. Maureen Hanson: Yeah. I'd like to comment that a number of ME/CFS researchers are trying to do what they can as far as medical education. For example, I gave a Grand Rounds at our local hospital and so there is some medical education going on even. But I do agree we need to get this into the medical schools, have them do a module that is specifically on, I would say, infection associated chronic conditions.

And maybe with the interest now in Long COVID that there could be efforts, joint efforts of people studying Long COVID and ME/CFS and chronic Lyme to have such a module.

Dr. Vicky Whittemore: If I could comment, I actually just had a call this morning with a group of clinicians from a Long COVID clinic at a major university and hospital in New York City who very much wants to develop such a training program for their hospital as well as one that could be utilized nationwide to really educate their providers, their medical students, the public, other primary care providers across the country. So there's significant movement in that direction and I think the best approach is what Maureen just said is to really expand it to these chronic post-infectious disorders, including Long COVID, ME/CFS, post Lyme, and others. So I think there's movement in that direction.

Dr. Cindy Bateman: Well, can I add one more comment? One of the things we're trying to do in furthering provider education is linked to Long COVID. And the CDC has funded an educational program, an online education program called Project ECHO that is on post-infectious illness, Long COVID and requires that part of the faculty be ME/CFS specialists. So those of us in the ME/CFS world are trying to collaborate and keep ME/CFS in the conversation.

Barbara McMakin: Great, thank you. We've received several questions in the Q and A box about what happens following the Council meeting in May. Dr. Whittemore, I don't know if you would like to speak to that?

Dr. Vicky Whittemore: Sure. So following hopeful approval of the report, I don't see why it would not be approved, it will go back to the Trans-NIH ME/CFS Working Group where we'll talk about where's the low hanging fruit, things that are easily implemented and sort of what are longer term kinds of research initiatives that may be needed to focus on research helping investigators to organize and to develop protocols for clinical trials. So it will, as I said after it's approved, the Trans-NIH Working Group will develop a plan for next steps that will hopefully also include partnering with several of our nonprofit agency or foundations and nonprofit groups to really help to foster research across the landscape where they can play a critical role in funding pilot grants as well that can provide initial support to investigators so that they can develop preliminary data to come in for NIH funding. So the report will not just be a report that gets put on the shelf to collect dust, it's something that will be actively implemented and will determine next steps following the approval in May.

Barbara McMakin: Great, thank you. How will NIH ensure that people with ME who are under the age of 18 are studied? I don't know if Dr. Hanson or Dr. Bateman, you'd like to take that one?

Dr. Cindy Bateman: That is a good question. It's much harder to design studies, studies in that range because there are higher expectations from the IRBs. So they can be done, but they have to be looked at separately.

Dr. Maureen Hanson: Yeah. And the other fact is that the incidence is lower in that group than later. So it can be difficult for a lot of investigators to find adequate cohort sizes to do it. And again, just like with people over 70, there's some interventions that you wouldn't want to do that or some, you know, requirements of a study that you don't want to risk someone under 18. But there have been studies that have been done in that age group and I quite endorse the idea that we need to do more.

Dr. Vicky Whittemore: So we have a representative from the National Institute of Child Health and Human Development, NICHD, on the Trans-NIH Working Group and it's something they're very interested in supporting. We just don't see grant applications coming in proposing studies in that young age group.

We also, NINDS is also partnering with the National Heart, Lung and Blood Institute to really foster research on dysautonomia, POTS, orthostatic intolerance. And we significantly, we really are encouraging people again to study individuals within that adolescent, young child and adolescent population. So if people have an interest in those types of funding, at that type of

funding, you can contact me and I can also put you in touch with individuals in either of those institutes.

Barbara McMakin: Great. Thank you. How are these research efforts being informed by and interfacing with research in other countries such as the UK and Europe?

Dr. Vicky Whittemore: Maureen or Cindy, do you want to take that, or do you want me to take a stab?

Dr. Cindy Bateman: Go ahead and then I'll see if there's anything else to add.

Dr. Vicky Whittemore: So we had Richard Simpson and Simon Carding from the UK as part of the Working Group of Council. And we are going to have a large part of the conversation at their upcoming Invest in ME conference, is going to be focused on these research priorities that came out of our research roadmap effort, as well as thinking about clinical trials, how do we move forward with clinical trials and what do we prioritize if we're going to move in that direction.

As you may know, Richard Simpson at Invest in ME coordinates Emerge, which is a European medical, European ME research group that coordinates research on ME across countries in Europe. And I think we do a lot of outreach across the countries to find out what is going on in those other countries. I attend the Invest in ME conference and meet with those investigators from across Europe as well. So we're, I think we're making every effort to try to really foster that communication to understand what research is going on and to really capitalize on the strengths of the research in other countries, not just here in the United States. I don't know if Maureen or Cindy want to comment as well?

Dr. Cindy Bateman: I'll just make a brief comment, but unlike the past, there is a great deal of interchange in the, in the scientific community, in the clinical community, even medical education with Australia and New Zealand and Europe. And it's fun, right? I think it's very healthy and we just need a little competition going on, right, to get this, to get this race on the road, to try to get to our answers.

Dr. Maureen Hanson: Yeah, there's really an increase in the number of conferences in different countries where we can be communicating with other scientists. So there is one coming up in Portugal, soon there'll be one in the UK, there's been ones in Australia, there were webinars, symposia hosted in Germany recently, one hosted in Austria. So really there's quite a lot of interaction internationally and scientists are communicating with each other by doing this.

Barbara McMakin: Great. Thank you. Now we'll hear from a couple of folks who have their hands raised. Val Dennis, you want to unmute your line and ask your question?

Val Dennis: Yes. Oh, okay. Sorry about that. Can you hear me?

Barbara McMakin: Yes, we can hear you.

Val Dennis: Thank you. This is phenomenal. This is my first contact with all of this and I have ME/CFS so it's a lot of information. Hopefully my question won't be irrelevant or redundant, but I was wondering I saw that one of the, I did not see actually that some of the research questions or topics would be maybe differences in different races and how that might manifest in ME/CFS. So I was wondering if there was anything about that and just on the idea submission side, is there any way to access already submitted ideas to like kind of try and minimize redundancies or we just fire them off and hope for the best? Thank you.

Dr. Vicky Whittemore: We'll take your last question first and then you can answer the other question. So you can go to IdeaScale and we can put the link in the in the chat for everyone. If you go to IdeaScale you can see all the ideas without having to set up an account and to be able to submit ideas. But you also are, once you're there, allowed to set up an account so that you can either add your ideas or comment on existing ideas. That's the best way to see all the ideas that have been posted to date.

Your other, your first question then about races, I think that falls into probably what Maureen presented in overall and overarching, maybe wasn't explicitly stated yet in the research priorities, but certainly will be part of the report that it's critically important to take race and ethnicity into account because I think that has not been done adequately in the past. Maureen, do you want to comment on that?

Dr. Maureen Hanson: Yeah, in my overarching list there, the word demographics was what was referring to that. So you know race and ethnicity and actually NIH already requires when you apply for research funding that you indicate how you were going to include you know ethnicity, race, sex in your cohort. So it is something that any researcher submitting a proposal to NIH must take into account.

Barbara McMakin: Great. Thank you. Next we'll hear from a caller who has dialed in via phone. The last numbers are 125. You can go ahead and unmute your line and ask your question. Please dial star 6 to unmute. I don't see them unmuting.

So let's go to some questions in the Q and A box. Are you researching the role of the vagus nerve?

Dr. Vicky Whittemore: So I know, yes. So I know that there are NIH grants that are funded to look at that and we're open to taking additional applications in that area. There is also a very large Common Fund program called SPARC that has investigated the role of the vagus nerve and

innervation of peripheral organ systems. That is not disease specific, but that is providing tremendous baseline information about how the normal nervous system does that, that we can then build on to look at how that innervation and nerve supply to peripheral organs is carried out. There's a lot of interest in the brain-gut interaction with the idea that the vagus nerve is potentially the highway that takes information from the brain out to the peripheral nerves but also is taking information from the periphery including the gut back up to the brain. So there's a lot of research ongoing in that area as well.

Barbara McMakin: Great thank you. Is there research looking at using CD19 CAR-T drug being used to treat autoimmune illnesses, for ME/CFS? Are there plans to use AI, big data and other recent tech advances for ME/CFS research? I don't know, Dr. Bateman if you want to start off with the first part of that question?

Dr. Cindy Bateman: I don't know the answer to that question.

Dr. Maureen Hanson: AI is certainly one of, is something that's in the research priorities. It's something that was mentioned. I actually don't remember if the CAR-T suggestion has been in the research priorities. I'd have to go back and look, but certainly machine learning and AI are both are both in the research priorities.

Dr. Vicky Whittemore: I know that there are some groups that are already beginning to do that, utilizing the data that's available on the tool mapMECFS where you can access data and begin to use machine learning and AI to look at correlations and across, within a study, and across various studies. So that research is ongoing.

Barbara McMakin: Great. Thank you. I think we have time for one more question. Could you describe how you would study the occurrence, progress, and prevention of post-exertional malaise?

Dr. Maureen Hanson: Could you repeat that again?

Barbara McMakin: Yes. Could you describe how you would study the occurrence, progression, and prevention of post-exertional malaise?

Dr. Maureen Hanson: Well, a number of groups including our own have studied post-exertional malaise and you know, there's already a fair amount of literature about how to induce it. Unfortunately, as far as how to prevent it, that is a key question. A key question in research because it is one of the most disabling symptoms, unfortunately.

Dr. Cindy Bateman: I'll just add that there have been quite a few what we would call provocation studies, either with exercise or orthostatic stress, and trying to understand how that leads to consequences. We've done some, published some papers on the quality, I mean the

nature of, post-exertional malaise, but it's been kind of elusive right still to understand exactly what the physiology is. And right now our best prevention is not inducing it and helping people understand how important that is.

But I agree, and that's why the IOM criteria put impaired function and post-exertional malaise as the primary core criteria. And in most of the other case definitions as well. So I agree that we need to have at least something a little more directly discussing that in our recommendations when we get to that point right there.

Dr. Maureen Hanson: There is now some molecular information about the changes that happen after you have post-exertional malaise. And I think when more such information is gathered and analyzed, we'll be able to figure out what is it that makes someone with ME/CFS not able to recover from something that is simple for a healthy person to do. So I, you know, I quite agree that that's a really important question in the entire field is what is resulting in this phenomenon of post-exertional malaise?

Barbara McMakin: Great, thank you. It looks like we're at time today. Thank you Dr. Whittemore, Dr. Hanson, and Dr. Bateman for joining us to talk about the ME/CFS Research Roadmap. A recording and transcript of this webinar will be posted to the NIH ME/CFS website soon. In closing today's webinar, I'd like to remind you about our listserv. For updates from NIH, to be added to the listserv, please visit the NIH ME/CFS website which is www.nih.gov/mecfs and click on join our listserv.

As you heard from our speakers today, the Research Roadmap will be presented to the NINDS Council on May 15th. We will send out a reminder to the listserv before that meeting. The open portion of the Council meeting will be on NIH videocast. Thanks everyone for joining us today and have a great afternoon.