The long haul: Personal and scientific insights into long COVID with Julia Moore Vogel

Melissa Suran (00:08):

This is Science Changing Life, and I'm your host, Melissa Suran. In May of 2023, both the U.S. government and the World Health Organization announced that COVID-19 was no longer a public health emergency. But the pandemic still casts a shadow over the millions of people living with long COVID—a chronic condition defined by a range of health issues that develop or persist more than three months following an initial COVID-19 infection. Long COVID is understood all too well by Julia Moore Vogel, who manages The Participant Center for the *All of Us* Research Program, an initiative that aims to build the largest and most diverse biomedical database in history. Julia joins me now to discuss how long COVID has affected her life—both professionally and personally. Thank you so much for speaking with me today, Julia.

Julia Moore Vogel (00:55):

Yeah, thanks for having me.

Melissa Suran (00:56):

To start off, not only is long COVID a major part of your current research trajectory, but it's personal to you in a way that makes your approach to studying it very unique. So how has your experience with long COVID influenced your research on the condition?

Julia Moore Vogel (01:10):

Yeah, I've had long COVID now for four years and I was really inspired by other folks with long COVID who started and were some of the first researchers to demonstrate that long COVID had this amazing—in a bad way—impact on so many of us in the general population. And so, I really followed in their footsteps, the folks from the Patient-Led Research Collaborative, to think about how I could make an impact using the skills that I have on this condition that there's really no solution for. So I would say, I had the skills and I was just trying to figure out what can I do to help our patient community because it is not being addressed as much as it should be.

Melissa Suran (01:47):

And obviously, there's just so much we still don't know about long COVID, especially in respect to its symptoms. As of now, what research questions about long COVID are you still hoping to answer and what have you been able to find thus far?

Julia Moore Vogel (02:00):

One of the most challenging things about conducting long COVID research is getting it funded, so that's really been a very limiting piece for us. And we've really just launched our first study, and we've almost finished accruing now—and that one is looking at the use of wrist-worn wearables for pacing in long COVID. So this is the same idea as the way that you would pace

yourself for a marathon, that you have to start slower in the first mile than you would if you were only running a mile, except it's just for folks to get through the day without making their symptoms worse.

If you go outside what we call your energy envelope and overexert yourself, many folks end up with this physiological state called post-exertional malaise, where many symptoms are worse, and some folks call it a crash. It really just feels like your body is shutting down, and it's unknown how long it's going to take to get out of that. But there's sort of this threshold where if you go outside that energy envelope, you're in this crash and it's much worse; but if you can stay inside your energy envelope, then you can operate more functionally essentially. And so, what we're trying to do is test the use of wrist-worn wearables to be able to stay inside your energy envelope. And that really is knowledge that came from the patient community and specifically the myalgic encephalomyelitis/chronic fatigue syndrome community to the long COVID community where folks tried it. I learned it from them, and I said, "You know what? It'd be great to validate this so that we can translate this knowledge from beyond patient support groups to, hopefully, something that clinicians can recommend to their patients at a broad scale."

Melissa Suran (03:26):

I remember a press release about the study mentioning that you were still recruiting participants. So what's the current status?

Julia Moore Vogel (03:33):

We are still recruiting, and out of 450 devices, I think we have about 25 left. So if folks want to join, they can go to longcovid.scripps.edu. But even when we're done recruiting for the folks that we'll be giving devices to, we'll still have it open for folks that already have devices that can come and share their data and help us learn about long COVID and still take surveys that help tell us about their experience. And we can see if we can start to draw correlations between someone's activity and then whether they have a crash or not and start to develop—hopefully—wearable data guidance for people to say, "You know what? You're ahead of where you should be for the day, you should rest." That's really tailored to you. And that's sort of what the devices do on their own. But to have it be even more data-driven and more long COVID-focused would be great because the devices that are out there on the market right now are really meant for exercise, and our version of exercise is much smaller in magnitude than most folks. And so, it's really great to have something a little bit more chronic-illness-focused.

Melissa Suran (04:30):

What other aspects of the research project would you like people to know about?

Julia Moore Vogel (04:34):

For this one, we're really excited to start the data analysis phase. So we need to have three months after the recruitment is completed. And what happens during those three months is: Half the folks get a wearable device right away, and half the folks get one after three months. And we compare them both at three months to say, "Okay, what difference did it make to have the wearable device?" Then, everyone has the wearable for nine months, and the study is 12 months long in total. And so, we get to do within-individual comparisons for folks that didn't have the device for the first three months and then had it later, and then we're also going to be doing between-individual comparisons at that three-month time point, which is the preliminary endpoint.

The other thing I wanted to mention about our long COVID research is we're working, now, also to fundraise for clinical trials for pharmaceuticals to treat long COVID. And that's an area that also has been really under-invested in so far, and we're looking for any funding source we can get—philanthropy, et cetera—to be able to run clinical trials to really address the heart of the problem. We know that the wrist-worn wearables and pacing is something that's helpful for symptom management, but it's never going to get to the root of the problem and completely cure people, and we feel that we really need pharmaceuticals for that. There are a lot of great candidates out there and we just need the funding to be able to run the trials.

Melissa Suran (05:43):

Long COVID research and treatment centers have been popping up around the country at major institutes. What could they be doing better?

Julia Moore Vogel (05:50):

I think one of the challenges is there are no FDA-approved treatments for long COVID. And so, they can help folks manage individual symptoms and that's about it. I think their capacity is still really limited because it's very specialized care and a very complex illness and so, expanding capacity would be great. And then, collecting as much information as we can and sharing it with each other so that we can start to understand the different trajectories of the disease. For example, there's very little about what happens if you have it for four years versus one year and the biological differences. There's emerging data, but not much, about what happens—and at what point is it treatable versus not. There are some ideas that your immune system gets exhausted after three years and it's much harder to treat the illness at that point. If we have more data on that, we might have more of a sense of urgency to treat folks, and it just might affect the way that we do things. I think it's still really early days in long COVID treatment, in that “root cause” sense that I was mentioning. There's, like I said, a lot for management, but we don't know how to eradicate it yet—except by not getting it in the first place. But that's not always within our control.

Melissa Suran (06:55):

And as we know, long COVID can occur following any bout of COVID-19, but it's kind of a toss-up as to whether someone will experience it. Of course, while certain preexisting conditions may increase the risk, anyone can potentially develop long COVID after being infected with SARS-CoV-2.

Julia Moore Vogel (07:11):

There's a lot of different data about who is more susceptible. There's the CDC monthly data that comes out saying in each different demographic group, who is more likely to have long COVID. And in the United States, it's about 6% of all adults have long COVID right now, and it's much higher in transgender individuals and individuals with preexisting disabilities. Of course, women are more likely to get it than men as well, but really, the transgender and the disability communities are being hit the hardest by long COVID. And so, that's data that I think we otherwise wouldn't have—and it has nothing to do, necessarily, with specific medical conditions. But we don't really understand why there is more long COVID there. I sometimes wonder if in the disability community, it's because folks are more in tune with their bodies and their limitations already. And a lot of folks that get COVID say, "Oh, I'm totally fine. I've recovered. I just can't exercise like I used to be able to." So I would label that as long COVID; but the average person might not be aware or labeling it in that way.

Melissa Suran (08:09):

I have a question related to that in terms of what continues to be the most misunderstood aspects of the condition.

Julia Moore Vogel (08:17):

There are so many things that are misunderstood. I'm making a whole list in my mind—misunderstood by the general public. So I think one of the most misunderstood things is that you can have an asymptomatic COVID infection where you actually didn't even know that you had COVID unless you happen to test at that time, and you can develop long COVID from that. You can develop long COVID from a mild COVID case as well. A lot of times, there's this misperception that it's mostly folks that were hospitalized, but it can also develop from even an asymptomatic infection. So that's another challenge with people labeling their own illness as being part of a COVID infection if they didn't even know if they had it.

A misperception among even the medical community is about how to address the fatigue that's caused by long COVID in a lot of people. And there is a tendency to prescribe what's called graded exercise therapy—so it's the idea that you're doing a little bit of exercise and you're adding, you're adding, you're adding over time. And I mentioned before, the energy envelope concept of “you have only this much energy, you have to stay within your envelope.” Those two things are completely at odds with each other. You can't add and expand the size of your envelope; that's just not how it works. It actually makes the condition much worse. And many folks, myself included, got that sort of advice and it has made us worse. So it's really important for the medical community to understand that.

The other thing that's really important for the medical community and the population at large to understand is this is not a condition that is in people's heads—this is real and biological. There's a lot of evidence out there that we can talk about demonstrating the biological changes that are behind this, and that's why you'll see so many people in the long COVID community continuing to mask and take precautions alongside, of course, immunocompromised individuals as well. But we in the long COVID community know what can happen to you by getting a COVID infection—and we try very, very hard to avoid it. The other thing I'll say is just because you get COVID once and you don't get long COVID, does not mean that you're free and clear. You could get long COVID from any given infection; each one is a roll of the dice.

Melissa Suran (10:12):

I actually have another question related to misconceptions. What other symptoms, besides fatigue, are you concerned about being under-reported because people don't recognize them as signs of long COVID?

Julia Moore Vogel (10:23):

Well, there are over 200 potential symptoms related to long COVID, so it's hard to even assign. It's not a clear thing where it's like, "Oh, if you have chest pain, it could be a heart attack." It's a very clear correlation. It's so disparate that I think pretty much everything has a hard time being correctly attributed, unless you're really aware of having your COVID infection and what happened afterward. I would say one of the things that I think would be a surprise to a lot of people is GI symptoms. A lot of people have difficulty with eating foods that they've never had sensitivities to before, where they have to really change their diet, and that's usually through mast cell activation syndrome as sort of a subset of their long COVID. A lot of people get headaches—and some had headaches before, but they're more extreme, and so that could be

kind of a difficult thing to track and attribute. Another one is cognitive dysfunction. A lot of people say “brain fog,”—but many feel that brain fog is minimizing—but real difficulty with doing cognitive tasks that you used to be able to do.

One more I'll mention that goes along with the energy envelope theory is basically any kind of stimulus can be exhausting. Like, just smelling something, just hearing something, just watching a movie can be really exhausting for people with long COVID, and it's important to consider all sorts of exertion of energy in the energy envelope theory. Thinking takes a lot of energy; digesting food takes a lot of energy. These things that we take for granted when we're healthy can really make a huge difference to a person with long COVID.

Melissa Suran (11:52):

It almost sounds like some people with long COVID also developed some form of a sensory processing disorder.

Julia Moore Vogel (11:58):

Sensory overload can happen really easily, and I attribute it to lack of energy—but I can see it sharing some commonalities.

Melissa Suran (12:07):

Going back to symptom management: Which long-term symptoms seem to go into remission over time and which ones tend to stick around? For those persistent symptoms, do you think more about managing them rather than finding a cure?

Julia Moore Vogel (12:19):

So certainly, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and postural orthostatic tachycardia syndrome (POTS) are both infection-associated illnesses that have existed from many infections, not just COVID, and been—as far as we know—lifelong disabilities going along with them. There's some management that we can do, but they are very stubborn conditions to get rid of. And I don't have personal experience with POTS, so I can't speak to that too much, but I know for ME it's very easy to make it worse and it's very hard to make it better.

And so, there's early evidence that every time you go outside your energy envelope, you actually make it smaller. So you're basically being punished for anything you try to do, and a lot of times, the way that we overexert is things that we would consider essential. Like, I have to take my child to the emergency room, and that is major sensory overload and major exertion; but I just need to do that. Same thing with emotional exertion. I had one of my worst crashes when my grandmother died during the early years of the pandemic and I couldn't be at the funeral, and that was really hard for me. I didn't physically move, but just the emotional exertion of that can make things a lot worse. And so, that's all part of ME/CFS and having to manage that energy envelope piece. I would say that, for most people, if you get better within three to six months after your COVID infection, there's a possibility that you could be in remission, and it could come back. But I've seen a lot of people get better and not have it come back within three to six months. If you get past that six-month mark, generally it's a more stubborn version of the condition that we haven't figured out how to treat yet.

Melissa Suran (13:49):

I'd also like to take some time to discuss your role as the senior program director of The Participant Center for the *All of Us* Research Program. And what was the impetus behind the initiative?

Julia Moore Vogel (13:59):

Yeah, sure. So this is an NIH-funded, very large consortium where the goal is to create a nationwide cohort of over a million folks that are reflective of the diversity of the United States population, sharing information about their health. And so, it is already the largest and most diverse research database of its kind, and it's already fueling over 10,000 research studies, which I love. A lot of research programs will sort of hoard the data for the folks who collected the data to make the best discoveries, but that's not the approach that this program takes. We make it available to qualified researchers, and if those in the consortium want to do discovery work, we can only do it at the same time as them. And so, I love that. One of the other ways I sometimes frame it is that Ardem [Patapoutian], our Nobel Prize winner, has access to the exact same data as a high school student that I'm working with who's analyzing the data. And so, that sort of democratization of data access allows the best and the brightest all across the country to come and use this resource.

We hope that it's especially helpful for addressing health disparities—which, you know, it's hard to learn about unless you have a very diverse population enrolled. Since we have that population with about 45% of folks who are historically underrepresented in biomedical research, based on their race and/or ethnicity, we hope to be able to learn a lot about health disparities and then also fuel interventions that can help get rid of these health disparities or move us toward health equity. So that's the consortium as a whole. What we do at The Participant Center—and I'm a co-principal investigator with Eric Topol, who leads Scripps Research Translational Institute—we focus on making it possible for anyone across the country to enroll and remain an active participant in the program.

So a lot of research is done in a local community where you're at a health center, and you're enrolling your local population. So there are many of those partners involved in the program, and we're filling in the gaps between all of them—the folks in Alaska and Hawaii and North Dakota and everywhere across the country. And so, we focus on scalable ways to reach out to folks, make them aware of the program, and scalable ways to interact with them. Most of that is digital first, just by nature of the dispersion of that activity, and we try to do a lot of things where we can send things to the participants. So we send saliva kits in the mail, we send blood collection kits, and then people can go to any of over 2,000 Quest [Diagnostics] locations nationwide. We send people Fitbits, and they share information about their everyday lives in terms of their sleep, their activity, their heart rate. And all of that data can come together to create a really unique resource for folks to identify different patterns that just aren't able to be discovered unless all the data is in the same place.

Melissa Suran (16:34):

It's great that you have this huge data set that's so accessible and continues to grow.

Julia Moore Vogel (16:38):

Yeah, one thing that's really interesting about the accessibility is all the analysis is done in the cloud, so you don't have to worry at your local institution about having the storage and compute infrastructure for hundreds of thousands of genomes. You can just access it in the cloud and

manage it that way, so it's much more of sort of an on-demand model rather than getting the equipment and having it for years and years. You just use what you need when you need it.

Melissa Suran (17:00):

It sounds like this could apply to many other types of research indications, per se.

Julia Moore Vogel (17:04):

Other consortia, yeah. That's one of the things that is also great about it—it's disease agnostic. So we have thousands and thousands of people with cancer, thousands of people with migraines, thousands with long COVID and ME/CFS, but we didn't recruit for any of them in particular. And so, what's great about having it together is someone that is a—let's say, case for diabetes study—can be a control for a cancer study. And so, by having it together, you can reuse the data many, many times for thousands of different research programs.

Melissa Suran (17:33):

Now, looking ahead and at your work at Scripps Research from a broad perspective, if you could answer one question through your research, what would it be?

Julia Moore Vogel (17:41):

Well, for me, I really would just love to cure long COVID, along with everybody else who's researching long COVID. It's just impacted me personally in ways that I can't even describe how extreme they are, and I know that so many others are impacted by it as well, and I'm lucky that I can even talk about wanting to do it. A lot of people can't talk, can't eat; they can't even interact with anyone. They have to put blinders on when someone comes in their room to help to take care of their medical needs. And so, it can be really dire. And I feel like, given the knowledge and the skills that I have, I almost feel a moral obligation to try to help. My second wish, I think, would be to help improve health equity more in general through the *All of Us* Research Program and to help launch the careers of many researchers who can access this data and, hopefully, make discoveries that otherwise would not be possible.

Melissa Suran (18:32):

What would you say is the most rewarding aspect of your work?

Julia Moore Vogel (18:35):

The most rewarding part is when I have people in our long COVID study that say it's really helped them. That's what I really want, and that's why I work at Scripps—it's because I want to have a positive impact on the world. Another example I'll give is we wrote a review of all the long COVID literature in 2023—Eric Topol and I and two other folks, Hannah Davis and Lisa McCorkle from the Patient-Led Research Collaborative. It's been accessed more than 1.4 million times, which is amazing for a research publication, and we've had people say, "I brought this paper to my doctor's appointment, and my doctor took me seriously. They were minimizing long COVID before, but now that they see it in a real publication, they are treating me differently." And so, to even have that small impact on people's lives is definitely the most rewarding part.

Melissa Suran (19:19):

So it's important to still get excited about the small victories.

Julia Moore Vogel (19:22):

Yes. It's something I've worked on in my time here, actually, because you try and try for so long and then by the time you finally get the thing, it's like, “All right, let's move on.” But the team here has taught me I really should take a moment to celebrate and recognize all the work that went into it—and celebrating is a good thing to do.

Melissa Suran (19:37):

A bit earlier, you mentioned how you also work with high school students on long COVID research. What advice would you give to early career scientists, especially those who are interested in studying long COVID?

Julia Moore Vogel (19:48):

I think for long COVID, in particular, make sure that you ground yourself in the infection-associated chronic condition literature that's already out there. I think a lot of people have the—this is another misperception, actually, that I missed before—that long COVID is 100% percent new; we've never seen anything like it. Well, actually, for SARS-1, they did a follow-up 10 years after, and people had long COVID-like symptoms. And it can happen after mono, it can happen after many different things. And so, making sure that you're not reinventing the wheel is important to be efficient in your resources.

The other thing I would say is: The patient community is very valuable in terms of perspective for what needs to be done, what's helpful to the patient, and what the patient can do. Given that it's an energy-limiting condition, it's not the case that you can just ask whatever you want of the patient the way that you might in another study. For example, doing an inpatient study or even having an on-site appointment is not possible for a lot of people. You need to make the experience very participant-centric and offer things through asynchronous communication, for example, or bring a phlebotomist to the person's home if you really need to collect their blood. There are so many different things that need to be taken into account for this population that is not there, and a lot of other conditions.

Melissa Suran (21:06):

Even though COVID-19 is no longer considered a public health emergency, the pandemic—as we've discussed—really isn't over for many people. So from those who have long COVID to others who still have to tread with caution because their immune system is compromised, do you have any words of hope?

Julia Moore Vogel (21:22):

Well, on the scientific front, I'm hopeful. I've been saying for every year that I've had long COVID, we're three to five years away from having real treatments, and I just recently updated to three to four, so I feel like we're actually making progress. We're getting some clinical trials going. I’m definitely more hopeful this year about treating long COVID than I was before. For the pandemic broadly, I really worry for the people that are more vulnerable, and I think that the public health policies are not adequate to have the protection that they should for the greater population.

I think that masking has a strange perception in society that is undue, and I wish that more people had the attitude that they had in the very beginning of the pandemic where it was like, "We're all in this together. We're going to figure this out. We're going to help our neighbors." And

that has sort of fallen by the wayside, and it's really too bad that it's the COVID-cautious versus the not-COVID-cautious in a lot of scenarios. So I don't have a ton of hope about that, except find your community of people that are like-minded and get support from them—and that can really help sustain taking the precautions you need to as well as your mental health. I rarely leave the house because I'm mostly housebound anyway, but when I do, if I'm going to be around people that are not in my household, I will mask, for sure. So I'm one of the still COVID-cautious folks. The other thing that I guess I'll mention that is really concerning is the proposals for mask bans. It's a terrible idea to not let people that are vulnerable be able to mask. I am optimistic about the mask bans not going through, but it is something that I worry about for those of us that are at higher risk.

Melissa Suran (23:00):

And what makes Scripps unique, especially in regards to how it approaches long COVID research?

Julia Moore Vogel (23:05):

I think what's amazing that Eric Topol and Steve Steinhubl really pioneered here is bringing the research to the participant—making everything remote so that you can reach folks all across the country. And we really work hard to make it accessible in that way, and that's really crucial for the long COVID community, as I mentioned, given the energy limiting nature. And we're all over the country, and we're all excited to participate in research; and by having it be nationwide, we can engage a larger swath of the population rather than if it's a specific location. The other thing that I've really enjoyed about my time at Scripps Research is that it's meritocratic, and the good ideas can come from anywhere—and we can find a way to make innovative things happen and collaborate to do something that is good for society. It's not as much about who gets credit for what or who has what letters after their name; it's inclusive and collaborative.

Melissa Suran (24:04):

And that's a wrap on this episode. Many thanks to Julia for joining me today and sharing more information about long COVID, as well as initiatives in the works to better understand the condition. Be sure to check out the show notes for more information on the cutting-edge work at Scripps Research and exclusive content from behind the scenes. If you liked what you heard today, please subscribe or leave us a comment. Thanks for tuning in and catch you next time on Science Changing Life—where listeners come curious and leave informed.