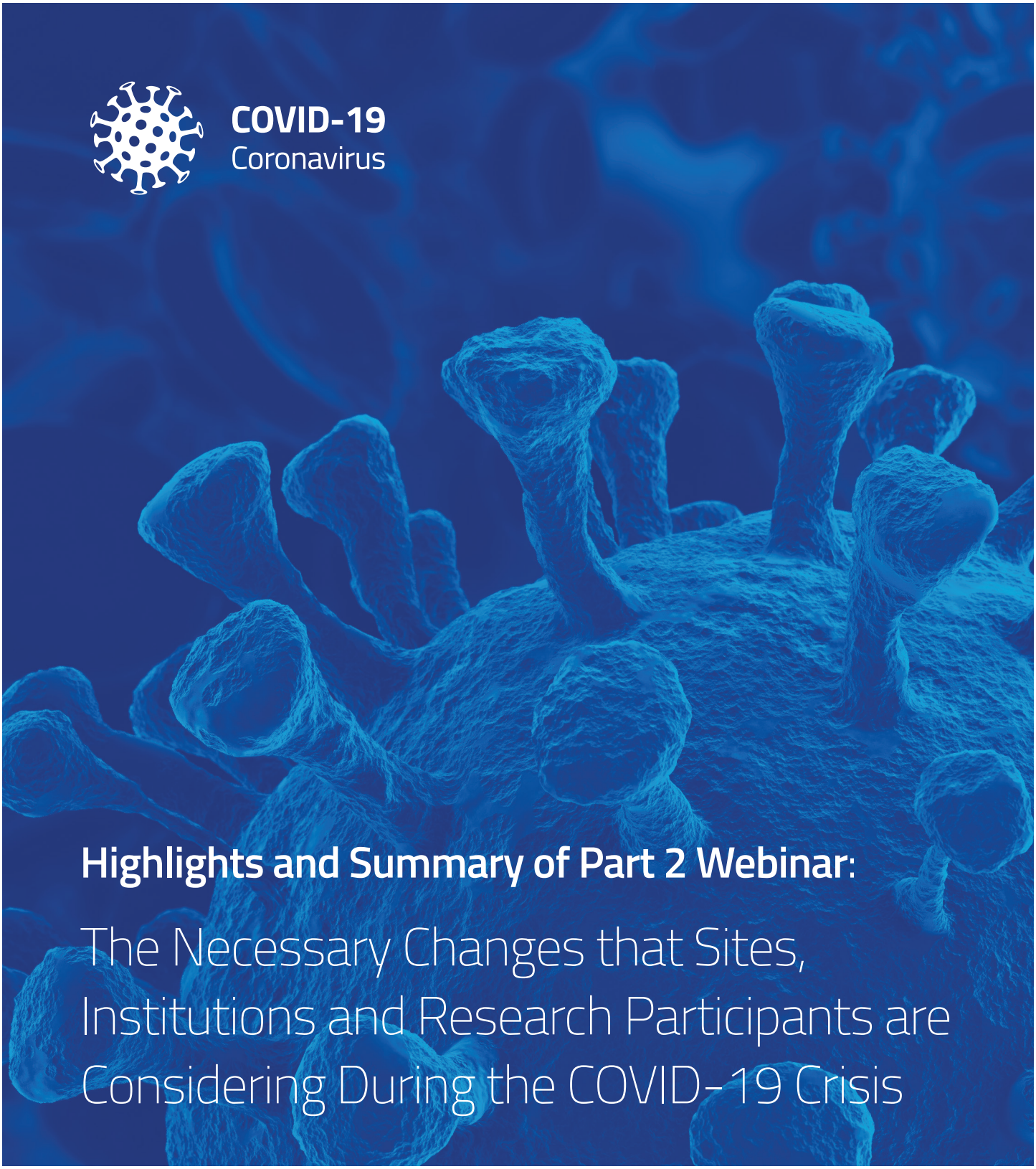

Highlights and Summary of Part 2 Webinar:

The Necessary Changes that Sites, Institutions and Research Participants are Considering During the COVID-19 Crisis

wcg™

"The coronavirus might kill me, but I know for sure my lung cancer will." -- lung cancer patient and phase 1 trial participant

As clinicians and site staff focus their energies on dealing with COVID-19, what's happening at clinical research sites? As sponsors delay or pause trials, what are the implications for research? For patients? And how do we work with participants and patient advocates to reduce confusion and uncertainty? Finally, what happens when the pandemic ends? Are sites and sponsors prepared?

As part of an ongoing series, WCG hosted a March 25 webinar to address these and related issues.

Featured speakers:

1. **Jonathan Zung, PhD,** *Executive Vice President, WCG*

2. **Lori Abrams,** *Senior Director of Patient Advocacy, WCG*

3. **Mary Elizabeth Williams,** *Writer, Speaker, Patient Advocate*

Lindsay McNair, MD, MPH, MSB, *Chief Medical Officer, WCG,* moderated

We have summarized key points and observations from each speaker, followed by questions addressed during the Q&A portion. You can find links to this webinar and an array of COVID-19 resources on our new **WCG Insights Program page.**

Decision-Making at Institutions and Sites in the Wake of COVID-19

1

Jonathan Zung, PhD,
Executive Vice President, WCG

From small independent sites to large academic medical centers to hospitals and site networks, research sites know the COVID-19 crisis will pass, and they're planning ahead.

Changes at Institutions

Nearly all institutions have issued internal guidances and most have posted them on their websites.

Overall, here's what we're seeing:

- Ethically appropriate and maximizes safety of study participants, research teams and the general public
- Primary focus on treating COVID-19 while pausing clinical research
- Research staff continue to shift from clinical research to supporting patients
- A pause in study procedures that involve in-person contact; non-clinical staff are working remotely
- Sites working with CROs and sponsors to
  - Ramp up remote monitoring capabilities.
  - Provide the access they need to see the data in real time.
  - Arrange access to study medication: Obviously in some studies it will be possible, to ship medications to the patients for oral dosage forms; infusions and subcutaneous injections are a bit more challenging.
  - Support participant engagement: Institutions are reaching out to study participants to provide them the information they need.
  - Make protocol changes, including changes related to data collection and patient visits.

Changes to Ongoing Studies

Participant visits should be performed remotely whenever possible. Sometimes it's not possible:

- Participant visits that cannot be performed remotely and do not provide immediate benefit should be postponed.
- Participant visits that cannot be performed remotely and are essential must follow enhanced COVID-19 screening measures.

Medication access: Arrangements are being made to provide study drug to participants at their home, where appropriate, but logistical challenges remain.

New-patient enrollment: Some institutions are allowing new-patient enrollment, provided

- The trial is essential to the participant's health—a cure or significant reduction of a serious medical condition.
- Precautions are in place to address the participant and research staff safety.

Learning on the fly
Institutions have implemented their business continuity plans, and we're hearing about what works and what doesn't. They are:

- Assessing gaps and how to meet the needs of study participants and sponsor/CRO requests.
- Working with study staff to support their needs at the study level.
- Engaging their providers and partners to ensure the continuity of deliverables.
- Planning activities for new trials are continuing. Many institutions have set up rules for which activities can continue.

Best Practices for Clinical Staff During COVID-19

Best practice for clinical staff during COVID-19, clearly first and foremost, is patient safety. Beyond that:

Maintain regular communication with sponsors and CROs to ensure effective bi-directional communication. This includes updates on changes at the site level and in the protocol as well as any new policies.

Ensure good communication with study participants. Keep participants informed on what has changed and what remains the same. They worry about their next visit. The worry about access to study medication.

Relay patient feedback and concerns to the sponsor/CRO.

Document which procedures are paused or being modified to avoid in-person contact.

Post COVID-19 Planning

There will be life and clinical trials after COVID-19. We've identified three key areas for planning:

1. **Develop plans for resumption of studies**
   - **Understand the status of all clinical trials:** ongoing, paused, discontinued, likely to be discontinued and pending.
   - **Know what changes were made to each protocol** due to COVID-19 and what will be required going forward.
   - **Assess your resource needs:** What resources will you need to support trials as they ramp back up? What can be handled internally? What needs external support?
   - **Determine how will you handle participant outreach and engagement.**

2. **Establish criteria and communication plans** for when to initiate new trials.

3. **Collect lessons learned:** At the organizational level, each site should conduct a COVID-19 lessons-learned assessment. What worked well? What could have been better?

Best Practices for Patients and Caregivers During COVID-19

2 **Lori Abrams,**
Senior Director of Patient Advocacy, WCG

Many of our patient participants have risk factors that make exposure to COVID-19 even more frightening. They are unsure of the future of their clinical trial participation; their new normal is changing again.

Sites can help:

Ask questions. Sites have direct contact with study participants. "I implore you, ask questions. We don't always know what people need, what they want and how they like to hear it."

Minimize anxiety about enrollment and randomization delays. Provide clear communication to people waiting to begin an ongoing clinical trial. Periodically check-in with patient participant and/or family member.

Mitigate fear and frustration with information. Patient participants need to understand their standing in clinical trials today.

- Will study visits will continue?
- Will screening and randomization appointments will be honored or postponed?
- Where will their study drug come from?

Clinical trial participants deserve regular communication from trusted sources, such as patient advocacy groups (PAGs).

PAGs Partnering with Sponsors/CROs

Many sponsors and CROs are giving PAGs timely clinical trial information about pauses, delays, modifications, etc., providing answers to questions best addressed by the sponsor.

Why incorporate advocacy into your teams?

- **PAGs have their finger on the pulse of the patient population.** They hear the questions and concerns that you might not be hearing.
- **They can help you develop communications** throughout this crisis that are not only patient-friendly but meaningful to patients and their families.
- **It's a way of getting your message across to a larger swath of your patient population.** For example, Colontown, a colon cancer group, holds

a Skype gathering each morning. They've brought all the different colorectal cancer communities, patient advocacy groups together and they share information, they're building guidelines together.

Becoming engaged with PAGs: Ask to join some of these advocacy groups in their daily or weekly talks--regardless of your study status. Don't wait to be asked by an advocacy group for help. Be proactive.

Develop resources: Once engaged with these groups, identify resources that are available to your patient participants. This is something you can put together as you're thinking about the communications that you're working on and include it in those packages.

How to Support Clinical Trial Participants and Families?

The ways you support participants and families may depend on your role in clinical trial development. For instance, sponsors don't have the ability to contact patients, but sites do. They can

- Help set up a buddy system (on their own or through an advocacy group).
- Provide routine, up-to-date information about the trial.
- Keep participants and caregivers apprised of policy changes. For instance, where on-site trials are still occurring, caregivers are not allowed in the facility. Sites can let participants and caregivers know ahead of time so they can plan accordingly. (Unlike in the past, the caregiver or friend isn't going to be able to duck into a coffeeshop for an hour or two.)

For those who work in advocacy or just want to pitch in, check-ins, shopping and ensuring people's needs are met are crucial.

The Patient Perspective--Managing Fear, Change and Messages About "Nonessential" Research Priorities

3 **Mary Elizabeth Williams,**
Writer, Speaker, Patient Advocate

"Very often when you come into this world as a patient, you feel like you've been slingshot into an alien terrain. You feel like everybody else knows what's going on and you are completely without a compass."

What follows are lightly edited excerpts from Williams's webinar presentation.

I talked to a woman today who is in her fourth phase I clinical trial and I actually wrote down what she said: "It became obvious to me that there were going to be discussions of who is worth saving and who is not. And someone like me, aged 60 with advanced lung cancer, would be put at the back of the line."

The gaps in healthcare will be illuminated: And I think that what's going to be coming ahead for us is those discrepancies, and the gaps are going to become clearer and clearer. We are all learning right now that illness does not take place in a silo, that it is not a compartmentalized experience and when we are dealing with communities where we are now also juggling our illnesses in new and deeper and much more challenging ways, our jobs and parenting, these kinds of challenges become even greater. It is very, very difficult to get a diagnosis or to live with a chronic long-term health condition. It is very challenging to leap into the unknown of a clinical trial or clinical trial enrollment. And then to pile on top of that, the uncertainty of what's going to happen next with your trial or with your enrollment is absolutely almost unimaginable.

A pause is not just a pause: I am respectful of all the unimaginable things that every single person on this call is dealing with. But I just want to speak to what patients are dealing with right now. That it is not just, "Well, I'm going to do this and then I'm going to do this and then I'm going to go with my clinical trial and maybe it will be paused." When we think about pauses, that is not an abstract concept for the parent whose child has a rare disease, who has been waiting to enroll in a clinical trial. That is not abstract to a 60-year-old woman who is on her fourth phase I clinical trial.

There is no time, there is no time for those people. And to put anything on pause is absolutely terrifying. And the woman I spoke to today said she has received no communication. She's received no assurances. And I really am grateful to every single facility and every single sponsor and nurse and doctor who is trying to

keep their patients and their participants in the loop as much as possible. We also need to be aware that that is not happening everywhere. Partly, that's because there's no information and partly, it's just the day-to-day problems with the healthcare system in general and the lack of communication we have been seeing before we had a pandemic.

The potential for lost confidence: But there are other concerns as well. I talked to someone else who was in a clinical trial that is very specific to mobility […] They're doing a lot on teleconferencing, but he is really wondering about the accuracy of, the validity of, this trial going forward. What happens when--in a trial that is going to be determining whether a treatment works for mobility issues--you can't test in the way he's become used to? How are these tests going to be compromised? How are clinical trials going to be compromised?

Do we as patients feel confident that, going forward, even in a best case scenario, we're going to be getting the best possible treatment? That those results are going to be the best possible? I don't know if that's a question that has been answered to the satisfaction of the patient community.

An opportunity to do better: I am hopeful when I look at this absolutely catastrophic experience…[that] we can use this experience to be better in so many different ways. I think this crisis has in so many ways cracked open so many of the systemic problems we have been having for so long. But within that, there is an opportunity to do better.

Research participants are on the frontline of healthcare, too: We are part of the story of research, we are part of the story of cures and the advancement of science and of health.

An opportunity for empathy: Very often when you come into this world as a patient, you feel like you've been slingshot into an alien terrain. You feel like everybody else knows what's going on and you are completely without a compass.

Sometimes it is very hard to feel like, "Does anybody else really understand what it's like to be this scared? To be this overwhelmed, to be this confused and not even have a voice, not even know what to ask, what the right questions are to ask?"

We're now in an unprecedented moment in our lives, in memory, in human history. And what that means is every single person on the planet right now does know what that's like. Every single person on the planet knows what it is like to have your life completely turned upside down in a very short span of time.

My hope is that every single person on the planet remembers that experience and uses it to deepen our empathy, to deepen our compassion, to make us have that moment of humanity in every single interaction that we have. So we […] treat the people that we work with not just as data points but as real human beings who are just scared and just vulnerable. And I very much appreciate that you are doing that and I'm very grateful for your time today. Thank you so much.

Audience Questions

Question for McNair

Lindsay McNair, MD, MPH, MSB,
Chief Medical Officer,
WCG

Q **When is it necessary to amend the protocol?**

A If you are moving from in-person study visits to remote visits, if you are planning to cancel study visits or discontinue patients early from the study or if you're planning to ship investigational product to people's homes as opposed to having them come into the clinic to pick that up, those would be things for which we would expect to see a change in research, a change to the protocol.

If changes are necessary to eliminate an immediate hazard to the safety of the research participants. It is possible to make those changes without preapproval from the IRB and to notify the IRB. Different IRBs may have different policies on that. Our policy is that we need to be notified within five days if a change is made in the protocol to eliminate an immediate hazard to participants.

It does not need to be a full protocol amendment. It can be whatever document you'd like to call it, a memo, a note to file, an administrative letter, whatever the document type is doesn't matter to us as long as it explains the changes being made, if there are any additional risks as a result of those changes, such as if study visits that were going to include physical exams will not anymore. So the IRB can assess the relative risks and benefits of those changes.

Jonathan Zung, PhD,
Executive Vice President, WCG

Q **You touched on the issues of what research was considered essential and used the term "direct benefit" in talking about studies that may not continue. Could you define those a little bit more explicitly?**

A In terms of essential studies, those are studies that provide high potential for direct benefit. For example, a cancer study for which there is no alternate treatment or perhaps a rare disease or cure of a significant disease. So that's what we mean by essential studies.

Q **Some of our listeners have heard rumors that sponsors may delay payments to sites. Have you heard of that happening?**

A We have not heard that. We reach out to well over 3,000 institutions today in our relationships. And we have not heard any of the speculation or rumors that sponsors may perhaps delay payments to the site.

Q **In situations where home healthcare services could be put into place to try to keep people out of the hospital site and possibly provide drug administration (e.g., infusion or injection) at home, who typically sets that up? How have you seen that work?**

A I don't know that there's anything that's "typical" now with Covid-19. We've seen sites working with sponsors or CROs to get that coordinated. I'd say it's being done differently depending upon the institution and we're aware of one or two institutions where they have satellite clinics and they're using those satellite clinics for that purpose. But I don't know that there's a typical approach. I think it's really being done on an ad hoc approach, institution by institution.

Q **So it sounds like maybe the best thing is for the sites just to make sure they're in close communication with the sponsor to figure out what the best way is going to be for that, in each setting and with each study?**

A Exactly.

Q **Shouldn't we just assume that sites are effectively just going to shut down and won't be available to conduct research?**

A No. There are a number of institutions that obviously are focused on COVID-19, but they're still planning to take on new studies once this moratorium on study starts ends. I mean we do anticipate study starts will start again. And institutions certainly are planning for that.

We're aware of a number of institutions that are working on budgets and working on different aspects of the study startup. So when sponsors are ready to start again, those sites will be ready to participate.

Q **We have been hearing about issues related to some institutional IRBs with clinician members. Those clinicians are now being pulled into the clinical care setting with such urgency that some institutional IRBs are having trouble meeting quorum; they have warned researchers that there may be associated review delays. Is that something that you have heard?**

A Yes. We're actively seeing that. Institutions are reaching out to us telling us they don't have a quorum and asking for active support from WCG from one of our IRBs. So obviously we've been working very closely with those institutions who require support so we can lend a hand.

Questions for Abrams

Lori Abrams,
Senior Director of Patient Advocacy, WCG

Q **Do you have any advice for sponsors or even for sites who are trying to find advocacy groups?**

A If you're a site within a community, the national groups often have local advocacy groups, local chapters.

For sponsors or CRO affiliates, my recommendation would be, first, before you do anything, check in with your sites to see who they have relationships with.

If there isn't an existing relationship, reach out directly to advocacy organizations that are supporting your disease state. You'll be able to offer guidelines and need-to-know information that can help their patient constituents. So don't be afraid to reach out.

The same applies to sites. Advocacy groups are busy, but I think that they want to partner with you. My recommendation is always to ask them first what you can do for them and then ask them or tell them what you need from them.

Q **What would you recommend for patients and research participants who are not part of an active advocacy community and don't necessarily have that community to rely on for support right now?**

A So if there isn't an active patient advocacy community, consider an "umbrella-like group." In the rare disease space, there are groups like the EveryLife Foundation or Nord or Global Genes. And underneath there is a plethora of people who have rare diseases, advocacy groups who have rare diseases. And so you have that silver thread that goes through all the different groups, that there are commonalities because everybody has rare disease.

In oncology, another example, you could go to something like the American Cancer Society, "but I actually would think about something more like the Cancer Support Community who really has a lot of resources from education to information about COVID-19."

And then lastly, The National Health Council in Washington, D.C., is an organization that really covers the whole depth and breadth of diseases and clinical trials and other components of healthcare and policy and rules and clinical trials that affect people with different diseases. And it really is an excellent resource for people. Something similar would be the Milken Foundation, FasterCures. Anyone that has a larger organization where you can really go and find either mentors or like-minded people, that's a good place to start.

Questions for Williams

Mary Elizabeth Williams,
Writer, Speaker, Patient Advocate

Q **There are people who have waited a long time for a study to start. They're finally enrolled, and now someone from the site has to let them know the study is being paused because it is considered "nonessential" research. What advice do you have for researchers or site staff who must have conversation with the research participants?**

A Well, for the love of God don't use the word "nonessential." I would say that's first and foremost. Very often the language that is used in the clinical world feels absolutely devastating to the patient population, to be referred to as "human subjects." And I really do so appreciate that you guys never do that. And that you call us participants means a lot. Language means everything. I cannot overstate that. The words you use matter. So I would be really working very hard right now and prioritizing the language that we're going to be using going forward. Understanding that of course hard choices are going to have to be made. And that is, by the way, not new.

We all understand that the American healthcare system is not fair and that choices are made about who gets to the front of the line and who goes to the back of it. But I would be really, really looking long and hard at the language that is used and understanding that it is very important to always put first and foremost the dignity and humanity of every single patient. I would be thinking about ways to have conversations that say we will support you in it. "Here are other things we can do. Here are your options, here is hope," but to never ever make a single person feel minimized in this absolutely terrifying moment when we are all so afraid of losing our dignity and losing our humanity and feeling like our lives don't matter.

Q **What do you hope this current crisis can teach us about how clinical trials could be better recruited and conducted in the future?**

A I think if there is one thing that has become abundantly, abundantly clear over the last few months and certainly the last few days, it is the absolutely urgent necessity to include people with comorbidities in the conversation and in the research.

We have seen what this virus is doing to the most vulnerable of our population and we have seen how absolutely terrified out of their minds people who have preexisting conditions are right now and yet so often clinical trial recruitment goes for the healthiest except for [the condition being studied].

How on earth are we going to fight this virus or any other serious illnesses and long-term conditions unless we are looking at the real patient population? Unless we are looking at people who are actually out there living in the world and already have one existing condition going on?

My deepest hope is that we take that seriously and that we are changing the game in terms of clinical trial recruitment to include people like that.