Transcript

Christine Bevc:

... Research Review or R3 Seminar. My name's Christine Bevc, I'm a senior research analyst and study manager with the RECOVER Administrative Coordinating Center, and I'll be your moderator for today. The goal of this seminar series for those of you joining is to catalyze a shared understanding of the research within the RECOVER consortium.

I want to start by thanking everyone who submitted questions in advance and remind everyone, as Cameron mentioned, that you can submit any questions during today's presentation and panel using the Q&A feature in your Zoom menu. And then after today's panel, our speakers will answer as many questions as possible if we run out of time. The Q&A document is also going to be posted with the recording of the seminar on recoverCOVID.org. The document will include the answers for submitted questions relevant to today's presentation. Questions about other scientific topics are going to be addressed in future seminars upcoming. And answers to any of broader questions about RECOVER are going to be available in the FAQ found on recoverCOVID.org. And then today as a reminder, as with our other past seminars, is that we cannot answer questions about individual clinical care.

All right, so next slide. So please join me in welcoming our panel for today. We have Dr. Kellie Owens and representatives Leah Castro and Rebecca Letts. Kellie Owens is an assistant professor in the division of Medical Ethics at NYU Grossman School of Medicine. She is a sociologist and empirical bioethicist who studies the ethical and social implications of health information technologies and is a former bioethics co-investigator for RECOVER.

Rebecca Letts has been a long COVID patient and pediatric long COVID caregiver since March 2020 when her youngest child brought home COVID from school, neither recovered afterwards. As an early long hauler, Rebecca became involved in multiple infection associated chronic condition and illness, IACCI advocacy organizations and projects, chiefly the COVID Hauler Advocacy Project, C19LAP. In June of 2021, she was recruited to join the NIH RECOVER Initiative Planning stages as one of our first pediatric representatives. She since helped plan and edit patient surveys, participated in the integrative physiology task force to help finalize study protocols and is currently a member of the NCEG Representative Engagement Subcommittee. In addition to her varied side projects, she's also participated in a number of manuscript writing groups in her role as a patient caregiver representative, co-author, consultant. Six manuscripts of which have been published to date on topics ranging throughout most of the RECOVER cohorts.

And also joining and rounding out our panel today is Leah Castro. She's been working with the RECOVER study as a caregiver and community representative since May of 2022. Since joining the RECOVER study, she's worked closely with the Health Equity Committee as well as the National Community Engagement Group, that's the NCEG subcommittees, including publications and health equity. Leah, alongside another representative, has also developed a standard operating procedure or SOP for the inclusion of representatives in the authorship process for manuscripts in August of 2022. She's currently one of the co-chairs for the National Community Engagement Group and the co-lead

representative of the NCEG Publication Subcommittee. Leah also serves on the Observational Consortium Steering Committee as a representative and on the NCEG Health Equity Subcommittee.

All right, next slide. So the topic for today's seminar is Ethical considerations in enrolling "invested parties" in large scale clinical studies: Insights from the RECOVER Initiative. Today's speaker and panel will discuss the ethical considerations for enrolling individuals who have a direct role in the study as study participants, including investigators, research staff or patient, caregiver and community representatives, and drawing from their experiences with the RECOVER initiative, they'll present an ethical framework for enrolling in invested parties in research. So please welcome our panel and with that I'll turn it over to Dr. Owens to provide some background and highlight some changes in the field. Kellie?

Dr. Kellie Owens:

Great. Thank you so much. I am thrilled to be here and to present some of our work today. So I will share some slides and get started it.

Okay, I am going to assume that everything's working. Stop me if it is not. But yeah, I am excited today to share some work from RECOVER that's probably a little bit different than what you might be used to hearing about in these seminars. So I want to talk about some work that came from my time working as a bioethics co-investigator with my colleague, Brendan Parent, at NYU, which relates to ethical considerations for enrolling invested parties in large scale clinical studies like the RECOVER Initiative.

So to jump in, I first want to just start by talking about how this issue came to our attention and what kinds of issues we're referencing here. So as you surely know, RECOVER is a very large multi-site study, which means there are lots of locations and rolling participants working with their own institutional review boards, which are the primary oversight and ethics review boards for research in the United States. And at one of the RECOVER sites in the Midwest, a principal investigator, someone who oversees the RECOVER study at that site, had a question about what he saw as a bioethics issue in the study. So basically he wanted to know if he or other members at his site who were working on the research study could also enroll in RECOVER as participants in the study that they're also then in charge of overseeing or working on in some capacity.

So he had reached out to us, first to Emily Anderson, who's an ethicist who worked with us on this manuscript, and then to Brendan Parent and I as the bioethics co-investigators for RECOVER to see what we thought of this issue because his site had identified some pros and cons, basically, for allowing study staff members to enroll in studies they're working on. And for background, when I say that they reached out to us, we knew that different RECOVER sites were at different stages of startup and recruitment. Other site investigators had also started talking to their institutional review boards about different kinds of enrollment. And to sort of spoil the ending a little bit, leadership ultimately decided that it would be left up to the local site level and their own individual ethics boards and institutional review boards to decide for themselves when and how they could enroll study staff in RECOVER.

But at the same time, they also asked the ethics team for guidance and key considerations about the benefits, the risks and best practices for enrolling investigators, staff and community representatives in RECOVER. So we wanted to consider that question. I'll talk a lot more about some of the key issues that come up here, like things about minimizing undue influence or coercion or how to safeguard privacy and confidentiality.

I also want to start with defining some of the terms that I'm going to be using throughout the talk today. So first, we're defining anyone who works on the study in some capacity, whether that's as an investigator who's involved in scientific design and implementation of the study, or a staff member who's more involved in the day-to-day operations of this study, or a community representative as invested parties. So you'll hear me keep referencing that. So they're in some way already invested in the study before they consider participating themselves as participants. So we want to understand what considerations arise in that dual role. And then I'm also referencing community representatives by which I mean patient caregiver or community members from groups most affected by a disease or an intervention who are then asked to provide feedback and are also involved in study design and implementation in some forms. And we'll hear, as we already heard, from some of the recovered community representatives who worked with us on this ethics manuscript a little bit later.

And I also just want to say that when this issue came to our desk, the question seems to have come because there were invested individuals who wanted desperately to enroll in RECOVER, not because we were hearing any concerns about recruitment or problems with coercion or something like that. It was really folks interested in enrolling and wanting to know whether that was okay.

So I want to start with a few vignettes that we've used in this manuscript because I think it might not seem obvious at first what kinds of situations could arise from enrolling invested parties in research. And I want to prevent four different vignettes from the paper that are at least loosely based on real scenarios that arose in RECOVER. Some of these details are changed, but here's the first example.

So study participants complete neurocognitive exams like the Mini-International Neuropsychiatric Interview, a brief structured diagnostic interview for major psychiatric disorders that asks a lot of highly personal and sensitive questions including about things like illegal activities like drug use. So study coordinators are trained to administer these interviews. They also know how they're scored. So study coordinators enrolled in the same study could feel uncomfortable administering or taking these exams with colleagues. If they're undergoing this testing as participants, coordinators could be attempted to either intentionally or inadvertently give particular answers because they know how things are scored, potentially threatening the study's scientific integrity. And this raised questions about whether invested parties might have either a preference due to privacy risks or an obligation due to risks around scientific integrity to abstain from these tests or to undergo this kind of testing at a different site or potentially to be disqualified from enrolling in the study if these kind of tests are a requirement of the study protocol.

So for us, this raised a lot of questions about whether enrollment of invested parties might also require some modified informed consent procedures to ensure that potential participants are aware that their sensitive data about their health and behaviors could then be accessed potentially by their colleagues that they work with. So in this example, we're really considering questions related to privacy, to scientific integrity and related to informed consent.

The second vignette we're mostly considering questions of fairness. So as part of their study role, a physician investigator calls subjects with some of their test results and answers questions they might might have and recommend recommends any needed follow-up care or helps them connect with their existing primary care or specialty physician for follow-up care. And the investigator is less comfortable making recommendations to colleagues that he knows well who are also participants in RECOVER or a similar study of this size.

So for example, a research coordinator participating in the study had an abnormal EKG that would require explanation and follow up. And the investigator here feels conflicted about discussing this with their colleague whom they're also casual friends. So they're concerned that they might either explain things in more depth than they would to other participants or make more firm recommendations because of their personal relationship with this person. And in contrast, other study participants would likely just be referred to their primary care physician to have a similar discussion. So this, for us, situation is a concern that an investigator might feel compelled to provide information to participants that they know and work with that would not be provided to other study participants. And there are questions there of fairness and also respecting the comfort level of the investigators to have these conversations with people they know.

The third example relates primarily to issues of privacy and confidentiality. So here a research study coordinator is also a participant, as are their partner and several colleagues. And the health clinic that employs that study coordinator and their colleagues has fairly strict policies about when employees can access their own or their family members' medical records in research processes. So this coordinator becomes worried that they're going to accidentally access records that they shouldn't, including their own or their families since a large volume of data will be reviewed in the study, many people will have access to that information. So they're concerned that they might enter a medical record number to pull up data not realizing it was their own or family members. And that is causing them significant anxiety about completing study tasks without breaking these rules.

At the same time, another investigator who reviews study documentation, including things like medical histories and laboratory results, came to us because multiple study staff and other hospital employees are enrolled in the study. And then the investigator then learns about their colleagues' medical histories when reviewing documentation. So here the investigator is uncertain about whether those colleagues know and are aware that the investigator has access to that information. And although study staff would know that investigators investigators review their data, other hospital employees may not, especially if this particular investigator might not be named in the consent form. So the investigator here is particularly concerned about finding out sensitive information like a diagnosis of anxiety or depression for example. And I think both of these questions raise concerns about whether there are additional oversight and communications about things like data privacy that might be required to ethically enroll invested parties in research.

And then a final example of the types of questions that came up in this example for us again focuses on fairness. So here, a study investigator is also a participant in the study and works at the hospital where study procedures and tests are done. So since the study investigator is not a principal investigator, the local IRB and hospital didn't have any policy prohibiting them from participating in the study. And as a result then they received monetary compensation for participation in the study just like other participants and for their time spent completing study tests. But since the study investigator lives

outside the public transit coverage area for the city, they get a gas card to cover the transportation and the investigator is questioning the appropriateness of this and feeling guilty even though they're being treated the same as other study participants, they're basically being compensated for driving to their workplace where they would otherwise be, which again they would do regardless of whether they were in the study. And then similarly, the study procedures are less of a burden for them compared to other participants because they're already at work. So this question was raised to us about appropriate payment structures for the participation of invested parties and about which types of special arrangements might be appropriate for their participation.

I want to turn now to existing policies. Given these examples of the kinds of questions and scenarios that were arising for enrolling invested parties in large clinical studies like RECOVER, we wanted to turn to the existing ethics and governance literature to see what people were already doing. So to summarize what ended up being a fairly large body of literature, there's really two types of existing policies at most institutions and they are policies for enrolling students or employees in research at their own institutions and then in self-experimentation.

So generally speaking, when we write policies about enrolling students or employees in research, we're worried about things like coercion and undue influence. So an example of that could be if a professor wants to enroll students from his own class in a study he's running, students might feel compelled to participate because they might think that it would help their grade or they're standing in the class, which we would consider a form of coercion that we've certainly seen many times in the past. So we're trying to avoid those scenarios.

And then for self-experimentation, I'm referencing scenarios like a scientist might develop a new vaccine or something and first test it on themselves. And in this case, research institutions are generally worried that scientists testing their own creations might not have an appropriate analysis of the risks and the benefits of their intervention because they're convinced it works, they built it, they believe in it. And in those cases we want to ensure that they're fully able to understand and consent to what they're doing. Lots of institutions just don't really allow self-experimentation if they can spot it.

And I want to give a couple of examples of these kinds of existing policies to give you a sense of what's already out there and what we were working with. So here's an example. It says, "Generally, investigators at an anonymous academic health center may not enroll themselves as subjects in the study that they're supervising. Such a practice presents obvious conflicts of interest issues and a variety of other ethical and practical issues like data integrity, welfare of the researcher, informed consent and oversight responsibilities." So in this case, this institution would not allow investigators to enroll in their own studies, although they do not mention here other staff or community representatives and how they might handle that group.

And then here is my second example of how another group advises research teams to handle the enrollment of invested parties, including patients and community representatives. So they say, "Principal investigators should not invite an institutional review board, should not permit patients and other stakeholders to occupy the research subject and study personnel roles simultaneously in the same study because of concerns about scientific integrity, by which they mean the potential for unblinding or other forms of bias and potential conflicts of commitment for those persons like if the person's own interests as a patient were to conflict with the aims of the research. But in exceptional circumstances

such as when a significant research would otherwise be impracticable or unable to be completed, the institutional review board may consider permitting the practice after consulting with relevant institutional officials and developing adequate protections appropriate to the circumstances."

So here again, the writers of this policy are prohibiting people from serving both as research participants and study personnel unless there are exceptional circumstances. I would say that this was a fairly common take that we saw. Although one thing that we learned in our literature review is that there actually isn't a ton of consensus about how and when enrolling invested parties could be allowed, which is in part why we wrote the piece that we did. So other institutions disagreed, and in some senses we disagreed with this policy, which is why you'll see that we have a slightly different take on this question. Although in the end we have very similar concerns, the ethics considerations are the same, we just fall in slightly different places in the end.

So now that we have some initial examples of different scenarios that can arise when enrolling invested parties, and we've done our review of the existing policies on these questions, then I turn basically to how my co-authors and I approached this question. So when we were thinking about what makes clinical research ethical, we often turn to what is perhaps the most classic framework in research ethics, which is from Emanuel, Wendler and Grady. They published in 2000 a list of seven criteria that are critical for the conduct of ethical research.

So to go briefly through these, the first is social or scientific value. So for research to be ethical, it should be able to improve health or wellbeing or increase knowledge, otherwise it really has no purpose. It should also be scientifically valid. So for research, again to be ethical, it has to use accepted scientific principles, methods to make sure that what it produces is actually valid and reliable data. Ethical research also has to include fair subject selection. So examples of that would include stigmatized vulnerable populations should not be targeted for risky research. And then the flip side, the rich and powerful should not be favored for potentially beneficial research. Favorable risk to benefit ratio is the next one. So here for research to be ethical, risks should be minimized and benefits should be increased and maximized as much as possible. And risks to research participants should be proportional to the benefits to those participants and or to society.

Another one is independent review. So here for research to be ethical, the review of the research trial should be conducted by individuals unaffiliated with the research to avoid conflicts. And then six, informed consent participants should know about the purpose of the research, its procedures, its risks and benefits, the alternatives to participation and any other relevant information for that study so that they can make a truly voluntary decision about whether they want to participate. And then finally, respect and potential respect for potential unenrolled subjects. So respect here means that participants should be, for example, allowed to withdraw from the research if they want to. We should be protecting their privacy and confidentiality. We should inform them of new research developments including new risks and benefits, new results. And then that we want to maintain the welfare of research participants as much as possible.

So in the case of our analysis of enrolling invested parties in research, what we did was literally consider each of those seven aspects of ethical clinical research and applied them to our case. So before I jump into these, I also want to say that we do this at a moment when medical ethics more generally is moving to a more permissive place. It used to be the case, and I'm talking here in pretty broad

generalizations, that if there was any perceived concern of conflict related to ethics concerns, folks in my field would tend to default to prohibiting that activity. And over time what we've learned is this approach can be overly precautionary and we can actually be preventing benefit to people by being overly restrictive. So now we often try and at least start from a place where we are trying not to preclude any activities unless there are really clear reasons why those activities are unethical or reasons why those activities can't be accommodated for some reason.

So that's our stance on this is we are attempting to be as permissive as possible while still protecting folks from unethical research practices. So when we think through the first requirement here, which is social or scientific value, we would consider would the categorical exclusion of invested parties violate the requirements for representativeness and inclusiveness in subject selection? And then suggest that if other ethical requirements are sufficiently met, invested parties should be allowed to enroll in research. So we're saying again here that our default position is that invested parties should be allowed to enroll because we don't want to exclude anyone unless there are particular reasons why their participation is inappropriate.

The second requirement is scientific validity. So could invested parties lie, for example to be eligible for participation? Or are the inclusion and exclusion criteria verifiable? Could invested parties manipulate their own data? And here we argue that what you need here is a robust screening process and that we can limit assets of invested parties enrolled in research to access their own data. That should in theory sufficiently manage threats to scientific validity.

The next requirement is for fair subject selection. So here we ask whether enrollment targets are sufficiently large in proportion to the population of eligible individuals that invested parties do not have disproportionate access to the benefits of research. So here we're suggesting that invested parties should not be actively recruited for participation, but also not actively barred from participation except in certain circumstances.

The next requirement is a favorable risk to benefit ratio. So here we're considering, are there any unique risks of research that might pertain to invested parties? There are some. So for example, might colleagues or supervisors have access to sensitive personal information? And here we suggest that if there are these unique risks such that the risk-benefit balance is not acceptable for invested parties, then they should be excluded. Otherwise, unique risks could instead be detailed in consent forms for invested parties and there may also be other procedures to help minimize those risks and protect privacy as much as possible.

The fifth requirement is independent review and I think this is a pretty important one. So here we're asking are there individuals with singular authority over the study design the inclusion of the exclusion criteria, the recruitment methods, data management, data analysis or reporting? And we're suggesting here that if you are an institutional review member already enrolled in the study, you should recuse yourself from ethics oversight of that study. You shouldn't have oversight power over a study you're involved in. That would be similarly true for data safety monitoring boards or DSMB members because they should not be allowed to enroll in a study where they're actively doing the data analysis and reporting. And then in some cases it might be desirable to also exclude principal investigators of multi-site studies from enrollment if they have the final say in study design and study procedures where we could see a real conflict of interest that could present itself.

The sixth and second to last requirement here is informed consent. So here we are asking, will allowing the enrollment of invested parties promote undue inducement or coercion to participate? And similarly do invested parties require additional information or decision support to understand the risks and benefits of their participation in the study? And are suggesting here that in addition to prohibiting direct recruitment of invested parties, so your boss should not be able to come directly to you and say, "Hey, can you participate in my study that really needs to up its enrollment," or something like that, we also need standard safeguards to be implemented to ensure valid voluntary informed consent. So an example of that could be informed consent of any invested party should not be obtained by someone with authority over that party. By which I mean again, your boss should not be the one conducting your informed consent procedure because you may not feel like you have as much choice in your participation. And then also an institutional review board may recommend engagement of a third party, like a research subject advocate for the informed consent process for invested parties to further reduce potential coercion or inducement by having a participant advocate in the room.

And then finally, our last ethical requirement is respect for potential and enrolled subjects. And our thoughts on this are a little bit lengthy, so bear with me. I know there's a lot of text on this slide. But generally we're asking will the study generate any data that won't be shared with all research participants such as tests conducted outside of certified labs that generally are not allowed to be returned to participants? And if that's the case, can invested parties access to this information be adequately restricted so they're not receiving information that other participants can access? Will other study personnel require access to this information in a manner that identifies invested parties potentially creating a conflict of conscience?

So here we have a number of additional safeguards that we think could be required, like depending on the tests being done and the procedures around return of results, it might be reasonable or desirable to prohibit enrollment of invested parties if there's a possibility of investigators or other team members having access to certain results that wouldn't be shared with other participants. So again, hear questions of fairness and if enrollment of invested parties is determined to be acceptable, it may be reasonable or desirable to prohibit the enrollment of statisticians data managers, really anyone with access to research-related results that won't be shared with participants. So that would include experimental laboratory or genetic tests, other things depending on the study itself that would help ensure that safeguards in place to limit individuals from accessing both their own and their colleagues' identifiable data.

So now that we have put our attention towards the various characteristics of ethical clinical research, we then wanted to provide some real practical advice and procedural guidelines for people making decisions about whether to enroll invested parties in research. So in some ways these are our key takeaways from our analysis. So here we are suggesting that the default presumption should be that it is generally ethically acceptable to enroll invested parties in research. Again, this is different although not completely out of line with other policies that we started with. And despite this default presumption, institutional review boards should provide explicit approval to enroll invested parties in research. So principal investigators should have to prove that they've considered that concerns that we've listed in this presentation thus far and that they have these appropriate safeguards in place. So it's not just a default suggestion for us that you can include invested parties, you really have to defend the safeguards that you're putting in place if you choose to go this route, even though we don't think they should be categorically excluded.

We have narrow criteria in the table above. That should be the basis for institutional review boards prohibiting enrollment of invested parties. Again, the idea here being that we want to default to including them except in scenarios where it might be inappropriate. And in the case of multi-site studies, if enrollment at another local site is a possibility, then this should be our recommended path over enrollment at your own site of employment.

And then our last slide of key takeaways and procedural guidelines is that despite the default presumption of acceptability, principal investigators can choose to categorically prohibit enrollment of invested parties, but they should justify and document this in the study protocol submitted for ethics approval. And there are a range of reasonable justifications here that we still want to carve out space for. So this could include if you just don't have the resources or the technical ability to provide appropriate privacy protections, then maybe enrolling invested parties is not right for this study. You might have a limited number of staff members to administer research procedures. You might have concerns about fair subject selection. There are a range of things here that we think could, for some studies, mean that enrolling invested parties is still inappropriate even if we are trying to open their potential enrollment.

So in only limited circumstances with strong justification, should institutional review boards be involved in determinations about the enrollment of a particular invested party, by which we mean a particular person. Instead, we want these decisions about enrollment of invested parties to be made and applied equally at least for each category of invested parties. So you might have different policies depending on the study for principal investigators or co-investigators, for study staff and team members or for community representatives.

And then finally, all invested parties enrolled in a study should be reported annually to the institutional review board and to the data safety monitoring board regardless of other reporting requirements. And this guideline for us is really to help us learn more about how often it's occurring that invested parties are also participating in research and tracking whether we notice any unanticipated problems as they occur so that we can revise this as we go. I am an empirical bioethicist, so it would be quite nice to have a little bit more data at our disposal to how this is going and if there are other ethics issues that we did not address here that we should consider as we revise this moving forward.

Here we go. So that is the end of our presentation. I am grateful for your attention. I want to thank all of my co-authors listed here. I'm certainly happy to answer any questions about this in the Q&A period, but for now I'm going to turn the floor over to some of the community representatives who worked with us on this paper as co-authors to hear more about their experiences and perspectives.

Christine Bevc:

All right, thank you Kellie. I'll invite our representatives to join us and turn on their cameras and mics. And while they're doing that, again as a reminder, if you can submit any questions that you have using the Q&A feature in your Zoom menu, and we're going to try and answer as many of those as possible. And just as we welcome our representatives, I think it might help our audience if we could

learn a little bit more about each of you and your involvement in RECOVER. We shared the bios at the beginning, but I think it would be great to hear a little bit more about what your roles have been. And why don't we go ahead and start with Leah?

Leah Castro:

Thank you, Christine. As you mentioned, I began working with RECOVER in May of '22, and since then I've served as a caregiver and community representative on the health equity committee, more specifically in the Communication Dissemination and Policy Subcommittee where I co-developed a standard operation procedure or SOP with my then-fellow representative, Jaleesa Thomas, to include all representatives patient, caregiver, and community on the development of the manuscript authorship process. In August of 2022, with the changes in the RECOVER engagement process, I joined the National Community Engagement Group or NCEG, which serves in the capacity of providing community partnership and engagement for lived experience and served as the lead of the Publications Subcommittee responsible for matching representatives to all manuscripts being published from RECOVER.

Christine Bevc:

Great. And Rebecca, your role's a little different. Can you share a little bit more about your own role on RECOVER and being a cohort study participant?

Rebecca Letts:

Yeah. My involvement at RECOVER started as a pediatric representative during the early planning period in June 2021 after I was recruited from one of the advocacy organizations. The long COVID communities that had already been working together for a while by then to get recognition and start the research process. And so there were people already aware of my family's situation and own awareness of the long COVID patient and community concerns. And so we started just in the planning process and basic RECOVER policies and then moved on to what would be in surveys. And when RECOVER actually began, I was placed in a task force. It was an integrative physiology task force and we did a lot that had to do with autonomic nervous system and other things that were multi-system tests and protocols for RECOVER. We were still planning going over tier two and tier three testing protocols and planning a number of other RECOVER things together.

In addition, my son and I around that time were able to participate and join into two different sites for RECOVER participants. He was in a pediatric one and I joined an adult one. So I also am in part of the NCEG Representative Engagement Subcommittee. And that is the committee I'm still part of and have made a lot of efforts with helping with manuscripts like this one, primarily in pediatric papers and

other ones that are relevant to the many conditions that my son and I have either developed from long COVID or have exacerbated from things that we didn't even know we had before.

Christine Bevc:

Thank you so much for sharing that. I think let's take a moment, and Kellie, we might need your help on this one too, is around just how RECOVER as an initiative has handled invested parties. We heard about the different ways in the presentation, but specifically for RECOVER, whether representatives can enroll and what that's looked like. And then we'll dig into some of the importance of that, especially in this case. I don't know if, Kellie, do you want to start us off? Or Leah?

Dr. Kellie Owens:

Yeah, I mean I can start by saying that in the end we do know that there are a lot of study staff and representatives who are also enrolled in RECOVER as participants. It was left up to the individual sites to determine with their own institutional review boards how that process should look. I will say that it's been about a year now, I think, since I have been formally involved with RECOVER. So I may not have the most latest enough to date information, but I do know certainly that there are invested parties enrolled and we have been, I think successfully managing any conflicts that arise from their participation.

Leah Castro:

Similarly, I would have to say I agree. I believe that patients and other nonprofit academic representatives should be included in research like RECOVER because their lived experience is vital to science and helping to understand real world challenges with this lived experience. People give real world input that they live with, which may have been left out of previous research. That being said, I believe that it is ethical because representatives do not design, develop or conduct the studies. They're merely participants.

Christine Bevc:

As a follow-up question to you, Rebecca, as a patient and caregiver representative, why was it important to you to be enrolled in the RECOVER study from your experiences?

Rebecca Letts: Yeah, and I apologize, I guess I grew rather faint and lost track of my thing.

It was really important for me to join because of my experiences and I didn't want others who knew long COVID patients and future long COVID patients to experience what my son and I experienced as early pandemic chronic illness patients with long COVID and associated conditions. That was something that was traumatic and basically impossible to deal with. And I had many privileges, countless ones including family and financial support. And I can't imagine what so many people had to deal with. And so I felt like even though it was so hard to speak up, I did.

So joining RECOVER as a participant, it was something I could do for the whole community. And as a representative, there's many things I can do to help those two things. I can go to the sites and bring back information to help, for example, in the task force plan, our protocols better. There were multiple situations where, for example, my first time going to a site visit, I was a bit disappointed because I do have POTS, postural orthostatic tachycardia syndrome, and they did a very abbreviated standing test where I only rested for five minutes and didn't stand for very long. And so my heart rate didn't have a chance to rest. And I could see that if I didn't know I had POTS and a number of other patients came in, that wouldn't have been caught and they wouldn't get the correct information they were looking for.

So I brought that to my task force, and of course we were actually planning autonomic testing for tier two and tier three later, but that was immediately escalated. And by the time I went to my second site visit, the resting was the appropriate amount of time and the standing was longer as well. And there were a number of times like that and in other things I could do to help the process.

Christine Bevc:

That's really invaluable, especially being able to have that continuous improvement or gaining knowledge and understanding in this Leah, are there other examples that you've encountered of how the representatives have been engaged in the process and been able to improve the studies that are taking place?

Leah Castro:

Oh, absolutely. I think just the fact that the representatives are included on the manuscript process to be able to input that experience that you don't get from crunching numbers, you don't get from looking at data, you actually get from living through it, that's invaluable. That input that representatives are contributing, you can't read any place. You have to live through it to be able to add it. And I think the mere fact that we have this system in place where we do have representatives involved on all of the committees, subcommittees and more importantly, manuscripts, I think that in itself shows how much of a difference representatives make. So yes.

Christine Bevc:

When you're saying how many, to give our audience a sense of how many representatives are involved? Because it's like we say committees and it's like okay, it's like oh, what size study? But I think if we have a number-

Leah Castro:

Right, Because we've added some more representatives to our pool, so I want to say right now we are at about approximately 115 representatives across the entire study. We've recently added about 40 something more, I want to say. Please don't quote me on the number, but I want to say we're about approximately 18 representatives in total right now. And we're making moves, we are adding and we are contributing and we're doing what we're supposed to do in our roles.

Christine Bevc:

Yeah, I think that really helps with some of the scale there, that it's not the two of you and-

Leah Castro:

Mm-mm.

Christine Bevc:

... yeah, no, it is much larger and it definitely speaks volumes.

Rebecca Letts:

Yeah, I would like to say there's so many and from so many different backgrounds all over the country and really so many backgrounds, it's beautiful. And also just working with people with long COVID and all of our associated conditions I think is helpful to the RECOVER staff and PIs. Day-to-day, we all deal with quite amazing situations. I was half blacked out and I was talking and this is the kind of way I work, and so it's an experience. And I openly share what my son has dealt with, what I have dealt with, all of our conditions and when we do the RECOVER test as a participant, all of that information that we have and all of the education that patients like myself have had to put ourselves through in order to get where we are is shared back and forth with the research and long COVID clinical community as well. And

that's why it feels really valuable in multiple ways. Even if there are some difficulties and it can be a slower process than we'd want, I think it's something that's valuable for the future.

Christine Bevc:

I was like that was the question I was going to key in on a little bit was the being the benefit of being in both of those roles as both a study participant as well as a member of the consortium. And Leah, I saw you come off mute there.

Leah Castro:

I did.

Christine Bevc:

Yeah.

Leah Castro:

I did. I mean just to piggyback off of what Rebecca just said, I think that each representative in respect of roles, everybody brings something different to the table, but together we work stronger. So we all work in the same groups, we support each other to again, piggyback off of what Rebecca just said, we have shared spaces where we just are able to just feel and express and it's just something special that's going on amongst the RECOVER representatives. There's something very special going on. And we get to work with wonderful investigators like Kellie to contribute to amazing science and manuscripts.

Christine Bevc:

So I want to expand a little bit on that, and you touched on it a little bit, Leah, too, but from both of your perspectives, because you're co-authors on RECOVER manuscripts, which are available on recoverCOVID.org, shameless plug. But if you can speak a little more about the role of representatives in authorship and in the publication process and what that's looked like on RECOVER, but also what that may have looked like if you have experience outside of RECOVER as well?

Leah Castro:

I can jump in. And then for sure, I would definitely want Rebecca to also give her input as well from the perspective of a patient caregiver representative included on the manuscript process. I know a different side to it because I helped to create the system that's in place. What role do representatives play?

Well, we are included on everything. We start with the publication process. We start once we're matched and it's a small subcommittee that does the matching of all the representatives onto the manuscripts, which is the Publication Subcommittee, shameless plug. We match all the representatives to manuscripts. They fill out a survey with interest of the different manuscripts coming down the pipeline. We then match them appropriately and according to how many manuscripts they're already published on or if they're brand new. Right now it is mandatory because of where RECOVER is that all representatives that are joining publish and participate in this manuscript process. Which brings me much joy because I love to see diverse voices on these manuscripts. So once they are matched, there's a kickoff meeting with the lead authors where the rundown of what will take place go through. So we get a more in-depth idea of what the paper will entail, what the cadence of meetings will be like, how we will be able to participate as far as what roles will play.

Then once the paper is drafted, after the analysis of data is taken place, we are also invited to those meetings as well. We start to circulate drafts of the manuscript where we kind of jump in on different parts of the manuscripts that we feel that we can most contribute best to. And sometimes it's something that we personally experience or we all have loved ones that personally experience, and sometimes it's something that the lead author may see something and will ask us, "Do you mind participating to this paragraph?" But either way, it is an amazing experience. And then we just wait for it to go through the IRB review process and get published. And then we are a part of science and history and it's been quite rewarding. And Rebecca, please jump in and give us your perspective now.

Rebecca Letts:

Did you have anything outside of RECOVER that you wanted to add?

Leah Castro:

I do actually. I work in other organizations outside of RECOVER. I work here in Georgia with the American Heart Association as a stakeholder. I also work with Emory on another COVID study. I also work with Mount Sinai, New York and New York Presbyterian, New York on different types of studies. And I also work with Insight as a stakeholder and with IHER at Mount Sinai as a stakeholder and valued member. And they all treat me as an equal partner. And again, it's an invaluable opportunity and it's

invaluable contributions that I'm very grateful to be available to participate in. Thank you, Rebecca. Now I cannot wait to hear you steal the show.

Rebecca Letts:

Let's see. Basically we can participate as much as we can participate there. I've seen every level and participated in multiple levels, all at a byline level. But I've seen representatives who wrote the papers, I've seen representatives who participate at completely equal level to the PIs. I mean, I have not. I've definitely written parts of papers, not big parts, but I've written parts. But generally, we can participate in the design, we can write, we can do what we can do. And also we can try to make sure we don't do too much because that's often necessary. Because a lot of what we end up doing is volunteering because of how long, at least for me, how long it takes to actually do anything with long COVID and how long it takes to think. But a lot of these are really important to get out there.

To contribute our knowledge and our experiences, I've had to, even right before a paper was published, I contributed maybe the very last word. And I've helped at the beginning when we were just trying to figure out where a paper was going. So I think that representatives are vital and I hope more research institutions take on patient caregiver community representatives. I think they would definitely benefit. The funny thing is when you start doing a lot of this, the general research community thinks you are a researcher. So I actually have reviewed papers outside of RECOVER.

I don't know if we're just talking about just our experience with authorship and the publication process. I don't come from a medical science background, so most of what I've written is not in this area. It's completely different and not recent. But I have done a lot of advocacy work and helped with a lot of different organizations. I wouldn't go so far as to say stakeholder. I don't know. Is it a stakeholder? But I definitely help with a number of different advocacy organizations and do what I can because that is very limited.

Christine Bevc:

Well, I want to take a minute to throw this back to Kellie and for her to also be able to share back what she's heard in RECOVER and that dual role that both of you have shared so generously. Kellie?

Dr. Kellie Owens:

Wholeheartedly, I'm tremendously grateful for the representatives we had that worked with us on this paper. At all levels, I think RECOVER is doing this incredibly well in comparison to a lot of other studies that I've been involved with at least. I'll back up and say that in empirical bioethics in particular, to write guidelines for what we think the right thing to do is we cannot do without talking to the people

that are actually affected by the conditions under study in whatever we're considering. So it's perhaps even more critical for us than it potentially is for folks who do research in other areas, but to be immediately connected to Leah and Rebecca and other people for this paper where we could ask them what are the things that you're seeing as you are living and doing the work that we're talking about here? We cannot write the paper without the perspectives of our representative authors on this paper.

So we had some ideas before we started. Again, going through these classic research ethics frameworks that can apply pretty universally across a lot of research, but how to apply it and what to consider for a particular project will always have to be pretty substantially informed by the people who know what they're talking about in a much deeper way than we do, frankly. We have, I think in ethics experience and tools in asking the right questions, but we cannot know the answers until we ask the people most effective. So it has been incredibly valuable to get their perspectives and to have them challenge us on when things are or aren't appropriate. And it's certainly something that I will take with me into other studies, is to try to build this resource. And include the budget for it too. I mean, it's not inexpensive to build this infrastructure, but I think it's so valuable that it will be certainly something that I bring forward.

Christine Bevc:

Thank you so much for sharing that. So we've got one last question and then we're going to wrap things up. And this comes from our audience and it's a general question, which I think it's like for recovered, there's that, but then also more broadly about this highlights the value of patient engagement and participants in participating in the process and caregivers and community representatives. How do people get more involved in the study other than just being on a trial? How can others become involved in studies like RECOVER? Oh, Leah, you're muted, if you were going to mention.

Leah Castro:

I was asking who were you specifically asking that to?

Christine Bevc:

I'm opening the floor, so if you want to start us off.

Leah Castro:

I became invited and involved with RECOVER from the work that I was doing in New York with Presbyterian and Sinai and one of the investigators and PIs that was working very closely with RECOVER, she recommended me and referred me to the engagement team who was then over RECOVER. And that's how I became involved with RECOVER, from the previous work that I was doing in the community and as a caregiver. So that's how I became involved. But I would say word of mouth. Reach out. The information on studies like RECOVER are on the website, as you plugged earlier, the information for the engagement team that oversees everything is there where you can reach out and just make your symptoms and your situation aware to them so that when recruitment begins again in the future, you are right on the top of the list to be considered to join the representative pool, which we welcome you and we are here waiting for that time to happen because it's a special place to be. But I would say to just reach out to the engagement teams. And it's public knowledge. That's what I would say.

Christine Bevc:

Rebecca, do you want to share how you became connected?

Rebecca Letts:

Yeah, as a patient, there are multiple ways. I guess the most common way would be through social media. And I know that there's a lot of controversy there, but not so much if you have chronic illness. Because if you have chronic illness, social media is your outdoors. It's where you socialize and see your friends and a lot of the places are actually closed groups, but in those closed groups you share studies or humor, ups and downs. But definitely studies to join and information. So much information. Conferences to go to that doctors don't have time to go to. And they're virtual. And especially after the beginning of the pandemic, a lot of them were actually quite affordable. So social media. I mean occasionally a doctor might share a good study, but it's not that often. And then there's ads. And then you can look them up on specific sites. What are some good ones? I don't know, there's a couple that just list studies, like government ones.

Christine Bevc:

Kellie, any other additional points on that one?

Dr. Kellie Owens:

No, I would totally defer to the representatives on this question. I think hopefully there's lots of ways to get involved. And the website would be my first place to head to, but I would again defer to the resources they've already shared.

Christine Bevc:

All right, be your own voice. Speak up.

Leah Castro:

Christine, if I may?

Christine Bevc:

Yeah, go for it.

Leah Castro:

I would also just suggest to maybe just ask your PCP. If you know that what you're experiencing is off, no matter if you feel like you're crazy or gaslight, advocate for yourself and just ask your PCP if there are any studies of what you're feeling that you can get involved in. Advocate for yourself.

Rebecca Letts:

And if they say you're fine and it's normal and you're still not feeling well, I know we're talking to mostly doctors here, but even if you're a doctor, it's still valid.

Christine Bevc:

All right, well this is going to conclude question and answer for today. I just want to say thank you again to our panel and thank you for the questions that we've gotten in from our audience. Cameron just flashed up our survey. While we are taking a moment to answer that, just as a reminder, a

recording of today's seminar is going to be available on recoverCOVID.org. That's going to be within a few weeks. We're also going to be posting the Q&A document that has the responses to the questions we received today, including a few that we weren't able to address publicly.

Now before we conclude, also just a reminder to researchers both within and beyond the RECOVER Initiative, you can now apply to use RECOVER data for ancillary studies. This includes data from three RECOVER cohort studies, so adults including pregnant adults, pediatric, and autopsy and bio specimens that were collected from cohort study participants. So interested researchers need to submit an ancillary study proposal and receive approval from our Ancillary Studies Oversight Committee. Researchers must also have independent funding support to conduct the proposed study. So to learn more, you can visit recoverCOVID.org/ancillary.

And also coming up... I was like I have the survey on there too. Next slide. We have also that we hope that you'll join us again for some of our R3 seminars. Keep an eye online, again, recoverCOVID.org for updates, and a list of those future seminar topics as we enter the new year. Additionally, if you haven't already completed that survey on there, take a minute to fill that out. And thank you for joining us and have a great rest of your day. Thank you.