# ADEPT-9 Enhancing Diversity and Therapeutics Development for Pediatric Patients

## FDA-University of Maryland CERSI Public Workshop

Moderated by Lily Mulugeta, Associate Director, Policy and Research, Division of Pediatrics and Maternal Health

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Building 31, Great Room 1503 (B+C)
Silver Spring, MD 20903

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A P P E A R A N C E S

List of Attendees:

Hilary Marston - Chief Medical Officer, U.S. FDA

Carla Epps - Senior Physician, DPMH, U.S. FDA
Director, Office of Medical Policy

Michelle and Michael Burgess - International Children's Advisory Network (iCAN) Parent/Patient

Christine Lee - Acting Associate Commissioner and Director, Office of Minority Health and Health Equity

Pam Simpkins - Managing Partner, Mezzopointe, LLC

Dionna Green - Director, Office of Pediatric Therapeutics, U.S. FDA

Lois K. Lee - Senior Associate in Pediatrics, Division of Emergency Medicine, Boston Children's Hospital

Sneha Dave - Executive Director, Generation Patient

Florence Bourgeois - Associate Professor, Pediatrics, Harvard Medical School

Ann McMahon - Regulatory Scientist, Office of Pediatric Therapeutics, U.S. FDA

Sue Rahman - Chief Scientific Officer, Health Data Synthesis Institute

A P P E A R A N C E S (Cont'd)

List of Attendees (Cont'd):

Rachel Randell - Duke University and Duke Clinical Research Institute (DCRI)

Ted Love (by videoconference) - Chair of Board of Directors, Biotechnology Innovation Organization

Bella Oguno - Vice President, Development Operations, Nuvig Therapeutics

Lauren Wood-Heickman - Clinical Reviewer, DDLO, U.S. FDA

Martha Donoghue - Acting Associate Director, Pediatric Oncology, Office of Oncologic Diseases, U.S. FDA

LaShell Robinson - Head of Diversity, Equity & Inclusion, Clinical Research Department, Takeda

Ki Lee Milligan - Executive Director, Pediatric Center for Excellence, Global Drug Development, Novartis

Stephen Balevic (by videoconference) - Associate Professor, Medicine and Pediatrics, Duke University and DCRI

Billie Jo Kipp - Clinical Psychologist, Indigenous Innovators Collaborative

A P P E A R A N C E S (Cont'd)

List of Attendees (Cont'd):

Lynne Yao - Director, DPMH, U.S. FDA

Tamorah Lewis - Division Head for Clinical Pharmacology and Toxicology, SickKids

LaToya Williams - Community Clinical Director, Inside Edge Consulting Group

Anvita Ambardekar - High School Student, Pediatric Perspective iCAN

Christina Edwards - Director of Clinical Trials, National Minority Quality Forum

Puja Umaretiya - Assistant Professor, Division of Pediatric Hematology/Oncology, UT Southwestern, Children's Medical Center

Melissa Penn - Director, Patient Engagement R&D, Bayer Pharmaceuticals

Nasrin Sari - Patient/Community Representative

Mathilda Fienkeng, Director, Office of Medical Policy

Jennifer McKenzie, Pediatric Nephrologist, Boehringer Ingelheim

A P P E A R A N C E S (Cont'd)

List of Attendees (Cont'd):

Heidrun Hildebrand, Pediatric Development Alliance Manager, Bayer

Melva Covington, Abundant Life Bible Church, AGAPE Strategic Solutions

Michelle McMurray-Heath - BioTechquity Clinical

Meshaun Payne, Support

Iana Zolkowski, Support

Reed Delisle, Support

C O N T E N T S

C O N T E N T S (Cont'd)

P R O C E E D I N G S

MS. MULUGETA: Good morning. We're going to go ahead and get started. On behalf of the FDA and the University of Maryland, Center of Excellence and Regulatory Science and Innovation, we welcome you to our ADEPT-9 Workshop on Enhancing Diversity in Therapeutics Development for Pediatric Patients.

My name is Lily Mulugeta. I'm the Associate Director for Policy and Research in the Division of Pediatrics and Maternal Health. I will be co-moderating this workshop with my colleague, Dr. Carla Epps, also from the Division of Pediatrics and Maternal Health.

Before I introduce the first speaker, I'm going to invite Dr. Lynne Yao, who is the Director for the Division of Pediatrics and Maternal Health, to quickly make a special announcement, and then we can get started with the rest of the agenda.

So, Dr. Yao.

MS. YAO: Good morning, everybody.

Thank you for joining in person. Really appreciate seeing all of you here.

So I do have a quick announcement. Actually, it made me think though. I'm sorry. I'm going to take the prerogative of the microphone of the bully pulpit, I guess, and just remind everybody that ADEPT-9 -- you know, does anybody even remember what ADEPT means? ADEPT means Advancing the Development of Pediatric Therapeutics.

And I had a conversation with our dear colleague, Diane Murphy, and this was about 11 years ago; okay?

And she said, "Well, we want to use these pediatric advisory committees for something that is, you know, more than just reviewing the ten-thousandth safety whatever prescription and review all the safety data at these pediatric advisory committees."

And we said, "Well, maybe there's another way to invite the community to come, not necessarily as formal as an advisory committee, and

start working on issues that are related to pediatric therapeutics development across academia, industry, and regulatory."

And that's how the ADEPT meetings began. And this would have been our 10th year. And the reason it's not is, because during the pandemic we missed one year. So next year, stay tuned, we'll have a grand 10th Anniversary ADEPT.

But I did want to give you that perspective. So this year, of course, another topic that I think is obviously important to everybody in the audience. So just wanted to give those brief historical remarks.

Now, the important -- and the reason I'm up here is to -- if you wouldn't mind looking at what you have on your table; I'm just going to read this.

"Please, be advised that the U.S. General Services Administration is conducting baseline water test at FDA's White Oak Campus and other FDA locations. This is part of a nationwide GSA

initiative assessing federal buildings of certain heavy metals and waterborne bacteria.

You may see signage posted at designated water fixtures or areas. Please, do not use these fixtures until signage is removed. Out of an abundance of caution, the FDA is recommending occupants refrain from consuming tap water at the White Oak Campus.

Where feasible, bottled water and/or water coolers are being made available for use." So there is bottled water for all of the participants today. I can assure you that all the food that's being prepared, the coffee, has been prepared such that it is safe to use and drink.

So I just wanted to give you that announcement in case you hadn't heard, and please, feel free to see me if you have any questions. Thank you.

MS. MULUGETA: Thank you so much for that, Lynne. So we're going to go ahead and move forward on the agenda. The first speaker is Dr.

Hilary Marston. She's the chief medical officer at the FDA, and she's going to walk in momentarily.

MS. MARSTON: There we go. Okay. Good. So I want to take a couple of minutes just to recap how we got where we are, where we are right now, et cetera, what the FDA has been doing in this space.

So the FDA broadly is committed to making sure that we get safe and effective medical products out to all populations, particularly including children.

We know that clinical trials are such an important part of this, and we know that clinical trials historically have inadequately represented diverse populations. We also know that they've inadequately represented children.

So when you take those two things together, you obviously have quite a problem that we need to take a concerted effort to address.

FDA is committed to doing our part to change this, but we also know that we only play one small part of the ecosystem, but we're doing what we

can, and we need the partners in this room to really advance this further.

So enrolling diverse populations, just want to take a moment to address what that actually means. So we obviously all think of racial and ethnic diversity, very important aspect of diversity.

We also need to think about clinical diversity; right? So what specific comorbidities might people have? What stage of disease might they be in? Also the conditions that they live in; right? So socioeconomic factors.

We need to have all of these aspects addressed in our diversity planning for these sorts of trials. So it's definitely not easy.

The reasons to do this are a myriad; right? So we want to make sure that the products that we have to treat children, that we understand how they're going to work in all populations. We need to be able to predict that.

We also know that it's the moral thing to do; right? So it is the right thing to do to make

sure that we are arming clinicians, parents, patients with tools that we truly understand as we're administering them to that. And the only way that we can do that is to make sure that we're actually studying.

So importantly, you got to plan for this; right? I mean, I know I'm preaching to the choir, but this is not something that happens on its own. You have to plan and you have to plan in advance.

So one of the things that the FDA has been calling for is diversity action plans across all trials. We also call for pediatric study plans.

In those diversity action plans -- we actually just put out a guidance on our thinking here, we want to ensure that trial preparers are thinking in advance, delineating the strategies that they're going to use, and thinking first about which aspects of diversity that they want to incorporate into their trials.

So you want to think about the patient

population that's going to be using the product. That might be different, obviously, from the patient population as a whole; right? So that's the first step.

Then thinking about the different challenges that individuals who might be using the products might encounter in their days and how to incorporate that into your trial. So we try to go through in a systematic way, ways that developers can think about it.

In addition, we had put out a guidance in 2020 to think about different aspects of development. So there, what we were talking about was really ways to think about the actual individuals that you were going to enroll in the trial and ways to think about eligibility criteria.

So moving forward, we have a number of other tools that we're using to look at improving diversity. These are tools, like innovation in clinical trials, for example, decentralized trials.

So we like to think about decentralized

elements -- the types of things that we can do in order to make sure that trials are more accessible to people.

So for example, if you're looking at rural populations, they might not have a clinic near them. These sorts of tools can be helpful.

All right. In addition, we want to make sure that we're thinking particularly about community engagement.

Community engagement for pediatric trials might well look different. We need to look at ways that we're going to reach not just populations broadly, but how are we going to reach their parents? How are we going to reach their caregivers?

The sorts of strategies that you might use in other trials might not be suitable for pediatric.

In addition, we want to think about ways that we're going to interact -- not just with the patient population, with their clinicians, with their communities, with their industry, with regulators.

So I think in this room we have the right people to take a look at these issues, to really dive into them, to come up with specific strategies, and looking forward to seeing what you guys come up with as we bring these two issues together.

So thank you. That's a little bit about where we've been; looking forward to knowing where we're heading. This is the group that will help us find that out. Thank you so much.

MS. MULUGETA: Thank you. So thank you so much, Dr. Marston, for that introductory talk.

Our next speaker is Mathilda Fienkeng. She's one of the directors in the Office of Medical Policy, and I'm going to invite her to come up to the stage.

MS. FIENKENG: Good morning, everyone, and thank you for being here. So as you heard, I am going to give you a brief overview of a workshop that was held in November of last year.

So first off, let me go; I have nothing to disclose. And as you heard Dr. Marston say, we

talk about clinical trial diversity. Why is it important? Well, clinical trials provide the critical evidence that determines whether a product is safe and effective.

And ideally, we want to make sure that the enrolled population, to the extent possible, reflects the diversity of the population that is going to use the product. And FDA is committed to this. And we do this through different means, which I'm not going to reiterate here.

In December of 2022, Congress passed the Food/Drug Omnibus Reform Act, FDORA for short. And FDORA had several requirements.

One was for FDA to convene a public workshop on diversity in clinical trials, to also publish a report on that; it also requires sponsors to submit diversity action plans, as you heard, and it required FDA to also issue guidance on diversity action plans.

So today, I'm going to briefly talk about those things.

In November of 2023, we did convene a two-day public workshop to fulfill that requirement. We solicited and received input on increasing diversity in clinical trials specific to underrepresented populations. The workshop attendees were very diverse, as you can see on the screen.

We also published a summary report on that, which is available online for you.

The topics that we discussed at that workshop were not specific to pediatrics of course, but while the discussions there were general and sometimes specific to other populations, those topics were relevant.

They are relevant for pediatric populations as well. And they will be complimentary, as you will see to what we are going to discuss today. But these are the different topics that were discussed, but I'll go in depth to them.

We talked about where we are now as it relates to clinical trial diversity. One key takeaway was the fact that despite all the efforts that have

been made, a lot of progress have been made. Some population continue to be underrepresented in clinical trials.

And also there were common barriers across these different populations. And those common barriers include distrust in research, not being referred to clinical trials -- some people are not even asked to join clinical trials, restrictive eligibility criterias, transportation issues, or providing clinical trial materials in language that is not appropriate for that person or not at their reading level, and finally, lack of community engagement.

I know I was sitting today with some advocates, but that community engagement was a key factor that was really talked about. And later on, you'll hear more. Now, efforts to address these barriers can help us to achieve that diversity in clinical trials.

During that workshop, the participants and the speakers covered strategies to overcome

barriers in clinical trials.

And one key takeaway was that sponsors need to diversify the trial investigators, the trial sites, and the trial staff. And this will help with better engagement and also ensure successful recruitment of that diverse population.

It was also key to provide language appropriate cultural literacy training for your trial staff, also being mindful of the lack of information, of lack of interest, or lack of trust in the clinical trial enterprise, especially in those populations that historically have been underrepresented.

Usually, we talk about building trust and having people trust the clinical trial sponsors, those conducting clinical trials.

But it's also key that those who conduct those trials demonstrate trustworthiness that way in turn, those who want to recruit can trust you, and they can enroll in clinical trials.

Understanding the population, the target population, understanding what that population

looks like, what politically, socially, economically, culturally, and of course engaging a diverse population must begin very early on, when you are still drafting your protocol.

You want to get those patient population involved at that stage. That way you are setting yourself up for success. And one thing that was reiterated over and over was to simplify the informed consent forms.

We talked about other strategies to overcome barriers, talking about employing targeted patient engagement plans, appropriately using decentralized clinical trial features and digital technologies, diversifying your clinical trial sites, optimizing your protocol, and also using patient concierges, if necessary, to help with scheduling and reimbursement for travel and transportation.

Now, when it came to establishing enrollment goals, which we'll hear is part of the requirement for the diversity action plans, the goals should be established based on the stages of your

clinical trial participation.

So because each stage has its own unique challenges, you want to match your enrollment goals to those. So you're thinking about the initial approach stage, the recruitment stage, and the retention stage.

Now, for devices, sponsors are encouraged to really think about the characteristics of various populations with the diseases so that early on in your device design, you can incorporate those characteristics and those factors, so engage with the engineers, the physicians, and the patients early in the planning phase.

An example is that historically women were excluded from some medical device trials, because the size of the devices limited enrollment of participants with smaller body sizes.

And lastly, appropriately leveraging different data sources. When you think about the prevalence of the disease that you want to use for your enrollment targets, use different sources to come

up with those disease prevalence data.

Now, many different approaches on including underrepresented populations were also discussed specific to subpopulations and in general.

One of the important aspects that was reiterated in that workshop was that we need to collect and track relevant demographic data in real-time. So you want to use a data-driven assessment as your trial goes along to think about that.

There are myths; there are misconceptions, and there are fears, and those need to be addressed.

One of the examples was the misconception that somebody, for example, with mental illness might not be able to follow or adhere to your study protocol or your study requirements or just excluding, for example, pregnant persons or persons with disabilities or those with complex health conditions.

So it's really about a paradigm shift, really shifting from this mindset of "Let's protect

this vulnerable population from clinical trials" to a mindset of more "Let's protect this complex populations with clinical trials."

So there is that need for that change in the ecosystem, and of course, providing education to those who are part of that ecosystem to take care of stereotypes.

Now, we've heard a lot about decentralized studies and digital health tools. When appropriately used, these tools can enhance the inclusion of a representative population in your trials.

So if you think about decentralized features, those may be useful when we talk about patients who are in remote areas.

You can leverage decentralized trials to maintain trials on certain times, for example, during a pandemic. You can use decentralized trial features during severe weather or during a war.

We can also incorporate those decentralized clinical trial elements in trials that

are conducted at the point of care. And that can help and enhance getting a diverse patient population.

It's important to evaluate the appropriateness of decentralized clinical trials and digital health technologies. For example, is there availability of broadband? What is the digital literacy of the participants you're trying to enroll in your trials?

In all of this, building that human connection is critical, regardless of what tools and what methods you use.

So after studies are done, it is important to communicate those data. We do not want the drive-by situation, where you come in the community, do the trials, take your results, and move on.

But sharing that information with the community, the patients will help highlight the importance and why it is important to have a diverse representation.

When you share that information,

protecting the privacy of participants is also very important. Transparency is important, using plain language, visual aids, to make that information more accessible and easily understandable, and putting procedures in place to make sure that the information you share is actually accurate information.

We have talked a lot about community engagement. It's important to really work collaboratively with the community and face with organizations. That way we are speaking to communities through a voice of trust.

Explain to participants why their participation in trials is important, and build that capacity in your overall diversity strategy.

And I cannot stress enough -- and in that workshop, bidirectional communication relationship with those communities are key as well.

So really to achieve that meaningful representation in clinical trials takes a village. It is important not only for the agencies, but for the sponsors, the clinicians, the patients. It takes a

lot of engagement and sharing of ideas, experiences, and best practices.

So we're going to shift gear briefly for the remainder of my time and talk a little bit about the diversity action plans.

This draft guidance was issued in June of 2024, and it met one of the requirements for FDORA. It actually replaced the April 2022 Diversity Plans guidance that FDA issued.

The guidance is actually still out for public comments, so I encourage you to read that guidance and provide any comments you may have. I have the docket number included on this slide.

So why? Why do we need diversity action plans? The short answer is to help improve generalizability of the results of clinical trials in an intended population. So the guidance actually assists sponsors in meeting the requirements for submitting the DAP.

So it describes the format and the content of the diversity action plan. It describes

the criteria and processes for sponsors who might want to request waivers, and also it provides general recommendations for sponsors to publicly post key information regarding the diversity action plans.

Now, which studies will require diversity action plans?

For drugs, a clinical investigation that is a Phase 3 study or, as appropriate, any other pivotal study of a drug, would require a diversity action plan.

For devices, any device, a DAP must be included for any investigational device exemption. And for those that do not require an IDE, the DAP must be included for a pre-market notification, request for classification, and application for pre-market approval.

FDA strongly recommended that you think about diversity action planning, the entire clinical development program, not just towards the end, but really we're saying submit them now, but we want you to think about them early on in the process.

What should be included in a DAP? Your DAP should include the goals for your enrollment, and those should be desegregated by age, by race, by ethnicity, by sex, so if you think about this for any clinically relevant study population.

You should also include a rationale for your goals, and explain how you intend to meet those goals. The guidance also describes the form and the content, as I told you, and it also gives you recommendations to help ensure that the requirements are met.

So I have here a list of some selected FDA guidances that speak to diversity in clinical trials, and just for your reference, I need to acknowledge my colleagues in division under different offices.

And I am looking forward to a day of learning and sharing with you all. Thank you very much.

MS. MULUGETA Thank you so much, Mathilda.

We're going to take clarifying questions during the panel discussions. Also of note, we're keeping the introductions very brief.

You have QR codes at each table, and you can access the bios, as well as the meeting agenda. For our online participants, the bios are available also on the event website.

Something that we've tried to do a bit differently with this workshop is really incorporate the voice of the patients and families throughout the agenda.

And we are really happy to have Michael and Michelle Burgess provide the KEYNOTE talk today. They are representatives of the International Children's Advisory Network or iCAN.

So Michael and Michelle, please.

MS. BURGESS: Good morning.

MULTIPLE SPEAKERS: Good morning.

MS. BURGESS: My name is Michelle Burgess, and I am here with my son.

MR. BURGESS: Michael Burgess.

MS. BURGESS: We want to thank you all for having us on today. Like it was currently said, we are representatives of the International Children's Advisory Network, affectionately known as iCAN, and we are so honored and privileged to be with you on today.

My iCAN family, I see a couple of you. Can you raise your hands out there? Hi there. I see you. Let's give them applause.

So everybody, let me just say this. I'm grateful to be here. I am so thankful for the participants and even the individuals that brought this all together. It takes a lot of work to bring a conference like this together.

So I want to thank Dr. Carla Epps. She's been so important in this work and helping to guide us. Thank you to Michelle Pollack, Ms. Jennings. Thank you to Robin Ruger [ph].

I haven't even seen your faces yet. I'm from Chicago, so I don't know a lot of people per face, but I want to thank you. Thank you to those who have made this possible for us on today.

So now that I have gotten all of the formalities out the way, let me just say this, this is my son's first public speaking engagement. So can you all make him feel right at home?

He's not in the hospital today. He is not behind a hospital door in a bed. He's standing with his mom.

So thank you, Michael. This is my dream to be with you like this.

So we have a presentation for you today. It's called "Enduring Hope." Please, go with us as we take you on a journey of Michael's life and how we have come through some very strong and challenging barriers to clinical trial engagement, but how as a family we have been successful.

So I'm going to start us off. It's going to be conversational in tone, and we're just going to go back and forth.

So Michael Julian Burgess, my son, was diagnosed with sickle cell SS at the age of 1 week old. Michael had his first pain crisis at age 8

months.

And I remember the doctors telling us that this is a time bomb; it's ticking, so you won't know exactly how the disease is going to behave until you kind of live it out.

So my husband and I were on pins and needles when he was first born, and the first crisis hit at just a tender tiny age of 8 months.

During that time -- this is in 2008, the hospitalization frequency was about maybe three times per year. So it was hard, but it was manageable. And Michael started treatments at Lurie's Children's Hospital at the age of 8.

MR. BURGESS: So throughout my life I've had multiple surgeries, starting at the age of 3 and most recently, about a year and a half ago, I just got my gallbladder taken out.

And ever since 2018, the hospitalizations have just been going up just drastically. It was told that it's probably because of me being a teenager and puberty, but we don't know

the exact reason yet.

And I began this new clinical trial back in April this year, and it's really been helping, and it's really made my life a lot easier.

MS. BURGESS: Thank you, Michael.

Now, let me just take the formal hat off. This is a picture of my family, you all. So it was a lot to even get us together to take this picture. You know, families are under a lot of stress these days, so just taking a picture is phenomenal; okay?

Michael thoroughly enjoys spending time with his loved ones and friends to help ease the stress of constant chronic pain.

So Michael has a tribe, and this is his tribe, this is his community. We undergird him when hospitalizations come. Even when clinical trial participation is a factor, we still undergird our son.

MR. BURGESS: So back in -- is it 2020? Back in 2020, when I was 12, I was recommended for this clinical trial, which I'm on right now, which is

really helping.

And I was next in line to get it, and then suddenly the FDA changed the age to 16, and so I was no longer qualified for the clinical trial.

And no matter what my parents said, no matter what I said, there was nothing that changed the fact that I had to wait another four years -- enduring pain for another four years, while the hospitalizations kept going up during -- with age.

And I started to lose hope that it was never going to get better. And I don't know how I was going to endure these four years, but with my family behind my back supporting me and my friends, I was able to keep going and finally made it.

MS. BURGESS: Thank you, Michael.

And so Michael has been a participant in several clinical trials during his lifetime. And so these are some of the barriers, the real-time barriers that I've heard some presenters already talk about.

Family/community distrust. So we come

from a larger tribe of family and community. We are deeply embedded in the heart of our community in one of Chicagoland's most underserved neighborhoods.

And so my husband and I are leaders there. And when we would, you know, discuss that we're going to have clinical trials -- we're going to enroll Michael in this trial, his doctor talked to us about it. This could possibly be something that could bring some relief. We don't know.

There was a lot of distrust that was already told to us -- that was communicated to us, "Well, why would you let your son do this? Are you sure? Do you remember," or "Do you remember what happened," you know, talking about, you know, historically what has happened in our black and underserved communities to our African Americans.

So that was hard to get through. It was hard to go to the hospital, finish that particular treatment for that trial, and to come home and to, "Oh, so you decided to do it; huh? You went against, you know, our better judgment; huh?"

And so the distrust, it was hard to overcome that barrier. The validity of suffering is something else that was hard to overcome.

Oftentimes, because Michael has what I call an "invisible disability," there are those who would say, "Well, is he really suffering; do you really need to go through this clinical trial," or, "Oh, my God," like, you know -- sometimes even hearing jokes just about the suffering and, "Does it really take all of that," that is a barrier. That's a mental barrier.

How many of you all know that comes and attacks your mental health when you hear those things. Distance, underserved communities. We live in Austin, which is a underserved Chicagoland community.

It's amazingly the largest community in Chicago with over 475,000 people that live in that particular area. It's well-populated, but it's underserved. That was a barrier to clinical trial -- financial constraints, job flexibility.

Some of the trials that Michael has

been involved in have required so much time off. And I have to pay a mortgage, just like you. So that was really hard, because sometimes our jobs were even threatened.

My husband is a high school principal at one of the top high schools in Chicagoland. I am also a district administrator. And our jobs were often threatened with the amount of time that we would have to give towards Michael participating in the clinical trial.

Financial participations and stressors -- I'm sorry, family participation and stressors. I have two other children, as you all saw on the previous slides. They have lost their parents. They lost their parents. And oftentimes that's something we talk about as a family.

So when my kids hear, "One more thing, ma; one more thing to manage," it's what we have to do. So that's a stressor.

So that's a barrier to clinical trial participation and just endurance, mental capacity,

just the stress of it all, and disappointment when we're not approved for a clinical trial. So these are all barriers that our family has had to face and had to overcome.

MR. BURGESS: So recently when I was talking about in April, I was able to qualify for the trial again, because I was turning 16, and a hope kind of reunited for me, because I was told that this clinical trial, like, really helped for sickle cell patients, and I was very excited to see what life actually feels like to be less in pain.

I'm still in pain, but it's a lot less than before, and it's a lot less frequent than before. And it's just been really nice to just have a little bit of stress taken off my life with this clinical trial.

And I still wish that this could have happened four years ago, but I know that life happens, and you just got to keep rolling with it, and that's what I'm doing right now.

And I was able to be a part of my

hospital's advisory board for kids. It's been, I think, three years now, and it's been nice to be able to advocate for other kids and just to be a big help in changing my hospital for the better.

And then I was able to go to the international version of that, the iCAN conference, for the past two years.

And that has been a really nice journey to be on -- to be able to travel and meet tons of new people that are going through similar challenges that I have and just to know that I'm not alone and that there's other people like me; and it's been very nice.

MS. BURGESS: Well, I want to talk about it. Michael just got his driver's permit. So can you all give my son -- that's huge.

I mean, it might sound like a little thing, but when you're a kid and you're struggling with a chronic disease that you're told you're going to die with, I mean it's -- the little things really help build that endurance of hope. And clinical trials is another thing that can help build our

endurance for hope.

So recommendations, everybody. We come to the conclusion of our presentation. So to foster patient and family engagement -- you all have said it already -- so I'll just reiterate it, access to medical resources in their communities.

So we live in Austin in Chicago, Illinois. There are very few medical clinics where we are. So Lurie's Children's Hospital is about seven miles from our home. It is a trek.

Michael's hospitalizations had spiked up to about three times per month, about four days each time. So the back and forth, it is just hard, so adding a clinical trial participation to that.

So that's what we need as real-time community dwellers. We need listening tours to ensure that our needs are met. I know that this particular public workshop is part of a listening tour.

Having our voices at the table saying -- you know, equity of voice, "Ms. Burgess, Michael, come to the table; we want to hear from you;

we want to hear what you're experiencing and what do you really need," that can help foster, I believe, success in any clinical trial and research.

Community town halls to educate communities on the impact and important of disease awareness. See, in our neighborhood the distrust is very high.

People would rather stay behind doors and suffer with their disease or illness, self-medicate, self-treat, than actually to go and see a physician until the situation is almost too late.

So we would really benefit from community town halls where hospitals and clinicians could send representatives to come out and gather us as a community and say, "Welcome to the table. Your voice and your opinion matters."

Finally, political will to eradicate systematic injustices in healthcare. We need you. Like the presenter before me said, this is bringing the human connection.

We need you. We need your expertise,

coupled with our lived experience, to really bring forth clinical trials that are really going to be impactful and effective.

Thank you all so much for this opportunity. I would like to thank Ms. Leanne West from iCAN, who is the president. I would like to thank her team, and I would like to thank all of you. I look forward to meeting you all. You are no longer strangers. You are friends. Thank you.

MS. MULUGETA: Thank you so much, Ms. Burgess and Michael.

It's really hard to believe this is his first time speaking in public, so maybe if we can give him one more round of applause.

Okay. Our next speaker is Christine Lee. She's the acting associate commissioner and director for the Office of Minority Health and Health Equity.

MS. C. LEE: Thank you so much.

Ms. Burgess, Michael, thank you so much for sharing your story with us. I think it's so

important to recognize not only your voices, but your lived experiences, as you mentioned.

You said a couple of key words in your talk that I hope that I can also highlight. Equity of voices, town halls, the bidirectional relationship, that connection piece, the humanization element, which I really hope that, you know, in this talk we also amplify.

And I also want to point out that I'm going to try to avoid word clouds with this talk and really focus on actions, which I think that everyone is looking more forward into.

All right. So I'm going to spend the next 20 minutes or so going over the FDA Office of Minority Health and Health Equity and the work that we have done to really advance pediatric health equity. Here's our standard disclaimer slide.

So the FDA Office of Minority Health and Health Equity, also known as OMHHE, our mission is to promote and protect the health of diverse populations through both research and communication

that addresses health disparities.

We also have a vision. This is, you know, my favorite vision, which is to create a world where health equity is a reality for all.

So what do we do in this space? I'm not going to go too much into the operationalization of the office, but we have two programmatic areas. We have the research and collaboration program, and we have an outreach and communication program.

The intent for all of our programs is to really connect with the communities that we serve and really advance health equity, including understanding the unmet needs of our diverse communities.

So as mentioned, I'm going to avoid word clouds as much as I can here. We all know the right words to use, equity, population health, health disparities. These are words that we all know to use. I want to try to avoid this and show you the actions that we have taken in the last three to four years.

In September 2021, we launched our

enhanced equity initiative, which really started this action piece when it comes to health equity.

In March of 2023, which is about a year and a half ago or so, we launched our Enhanced Equity Research Hub, which I talk about very briefly here.

But after talking to some of our audience members, I really think I should have had a couple extra slides here. But please, if I don't have slides here, come up to me afterwards, and I'll walk you through the Enhanced Equity Research Hub.

And a year and three months ago, we launched our newest initiative, which one of our PIs is here -- you hear from her in just a little bit -- Dr. Billie Jo Kipp, the OMHHE Racial and Ethnic Minority Acceleration Consortium for Health Equity.

The key term here is "acceleration," because many times we tend to talk about this, but where's the action and the acceleration to action?

So even though this is only a year and three months old, I think we've done tremendous work, thanks to our wonderful PIs that we have.

So going into the first action item here, which is the Enhanced Equity Initiative, the Enhanced Equity Initiative has three equity branches or three equity pillars.

The first one is equity in clinical trials, which is the topic of today, and I'll go into some of our projects in this space.

The enhanced equity clinical trial area looks at not only understanding barriers and unmet needs, which was shared a little bit earlier today around the clinical trial barriers, but also looking at strategies, especially community-driven strategies on what it means to increase engagement for your community.

We also have our equity and data efforts. As we know, there's a lot of missingness when it comes to equity of data. Many times without data, we don't know what direction we're heading in. Are we heading in north, south, west, east; right?

So really understanding our comprehensive data when it comes to our diverse

populations that we serve.

The third element here, which you know, I think it was meant to be, Ms. Burgess talked about equity of voices. This is also one of our equity branches.

The equity of voices is a two-part branch. The first part is really understanding the unmet needs. Ms. Burgess talked about town halls going into communities.

This is exactly what equity of voices has done through our community leaders, like Dr. Billie Jo Kipp here, for example, in the tribal nations, that she'll talk about in just a couple minutes or so.

It's really having the community leaders have these town halls. I always say that many times, if you don't have that trusted connection, why would someone share with you their unmet needs? There's no trust; right?

So many times when we do town halls that don't have that trusted element, what ends up

happening is that we get another word cloud, because there's the lack of trust.

So really having, for example, our tribal colleges, our HBCUs, our fairly qualified healthcare system docs, do the town halls, really connect with the community, what we find is there's a richness of information that comes out. Information that we may not have ever heard of before. The unmet needs really surface to the top.

The other thing with equity of voices is after we understand the barriers, the unmet needs, then we can better tailor communication strategies. For example, my sister, she's 10 years younger than me, we communicate very differently.

I have no idea of what language she's using half the time. So really understanding, you know, how the communication preferences need to be tailored.

Okay. So moving on, we haven't updated this for our FY24, but we will be soon. As you can see, the growth of the OMHHE Enhanced Equity

Initiative has grown tremendously from about 10 projects in '21 to now we will be topping at more than 60 projects, all which can be found on our Enhanced Equity Research Hub.

So here, I would really like -- I'm a very visual person, so I'd like to see the growth of our program. So what does it mean? Remember, I promise a lack of word cloud. So here's my stand-in.

So our enhanced equity initiative of FY21, our equity of clinical trials, what are the fruits of our labor here?

So, of course, I'm a Floridian girl, so I had to use oranges to set the example here. But as you can see here, this is the product -- the fruits of our labor over the last three to four years.

We are now at 24, not 22, clinical trial studies that look at the barriers for our populations. Looking at it from an age perspective, from a racial and ethnic minority perspective, from a rural perspective, from a tribal population perspective, it doesn't make any sense to clump

diverse populations into one bucket.

For example, I talked about my sister a little bit earlier. Although we're both Asian, her communication strategies are very different from mine. Her unmet needs are very different from mine. So it's very important as we're creating these tailored clinical trial strategies that we keep this in mind.

The other thing that Ms. Burgess mentioned a little bit earlier was the connection point. So having an ability -- a platform to connect with the FDA.

I'll show a couple pictures near the end of platforms -- environments that we have created at the FDA, as well as going into the community.

So we're trying to do one here, one within a community; one here again and one within the community, to really get the voices when it comes to meetings, workshops, listening to diverse perspectives.

Also, we have our OMHHE guidance document. Mathilda mentioned a little bit earlier the

diversity plan guidance. We also have our race and ethnicity standardization guidance document. And we also have our longstanding clinical trial campaign.

So here's our longstanding clinical trial campaign. Everything is publicly available. If you want free material shipped to you, we can also do that also.

But online, we have about 12 languages available. We have our fact sheets; we have our webpage; we have podcasts; we have webinars, that really highlight the importance and strategies on advancing clinical trial diversity.

Here's the guidance that I mentioned in one of the oranges. So this is our guidance on the collection of race and ethnicity data in clinical trials.

The purpose of this guidance -- I mentioned it a little bit earlier the importance of data -- the equity of data element. Without standardization of race and ethnicity data reporting, it's very difficult to understand what that data

means.

So this is our guidance on the collection of race and ethnicity data in clinical trials. The main point here is using standardized terminology for race and ethnicity helps ensure the data is collected consistently and supports demographic data analysis.

All right. So this was this past April for our National Minority Health Month. You'll recognize in the middle, in pink, Dr. Billie Jo Kipp, who is here, who will be speaking a little bit later.

But this was really a invitation from our communities, from our tribal nations, our racial and ethnic minority populations, our rural populations, to come here and share the strategies that work for their communities.

And what was very interesting was that there was very overlapping similarities in what they were saying, but very important, it was important to recognize the nuances too. So that was also highlighted throughout.

I mentioned a little bit earlier about the 60 plus projects that we have funded through the Enhanced Equity Initiative. This is just one that was tailored towards our young adults.

So here, this was a very interesting process. What we heard through the focus groups with young adults were, yes, we want to participate in clinical trials, but I don't want you to tell me what to do. All right. Second of all, but if you don't tell me, I'm going to be mad at you.

All right. So this is where I was like, "Oh, my goodness, I don't know what to do." So they took a bunch of these young adults and threw them in a room, and they're like, "Workshop it"; right?

So this was their creation, which I call "a dating app." So this is the clinical trial dating app.

So here, what the young adults wanted, they wanted to control over their preferences. So they would put in the app, "I'm looking for this in a clinical trial. I'm looking for this geographic area.

I'm looking for -- these are the things that are important to me."

And then the app would geolocate those preferences to a clinical trial that matched their preferences. So this is just one of the innovations that come through our Enhanced Equity Innovation Awards.

Dr. Ann McMahon will be talking about this in just a couple more minutes. But this is another way for us to really advance research, which is through our intramural grant funding process, which is funding our internal FDA scientists.

And here -- I won't talk too much about this, because she'll do a much better job than me, but her study really aims to highlight and test the hypothesis that children of racial and/or ethnic minority populations are underrepresented in pediatric clinical trials.

Moving on to the second equity branch are equity of voices. So what have we done in this space? So we have 17 Equity of Voices research

projects. Remember it's two parts. One part is really understanding the unmet needs, and the second part is the culturally tailored communication strategies.

We also have our Equity of Voices videos that are publicly available online, and anyone can access. We also have our podcasts and webinars. And we also have our language access program that focuses on translation.

So here's some of the work that's in this space -- our podcast, which is available online. If you're ever in a long car ride, please tune in. And here's our language access program.

Going on to equity of data, we have six projects within this space. And I just wanted to highlight that all of these studies actually contributed to the last orange right there, which is the Enhanced Equity Research Hub, which I mentioned just a little while ago. I'll get to that in just a little bit.

So for equity of data, when we talk

about equity of data, there's so many challenges in this space from the lack of attention of awareness of the racial and ethnic minority data in real-world data settings, the lack of, you know, understanding of potential covariates and demographic variables that can contribute to confounding outcomes, and a lack of attention to barriers that prevent reporting from racial, ethnic, and other underserved populations.

Missingness is a huge problem also. Sometimes the data sets that we look at have missingness from about 60 to 70 percent missing as when it comes to racial and ethnic minority information, which at that point, I'm not really sure what we can do with this data.

And then also there's that struggle with understanding prevalence estimates of disease population. Because of all of the challenges listed above, if you have such a high missingness, how can you calculate the prevalence of the disease?

Oh, okay. All right. So this is an area that -- you know, one of the studies that we did

was we funded a study with Stanford University with Dr. David Rehkopf of Stanford.

And he really looked at understanding the American Family Cohort database, which is the largest EHR data set on primary care in the U.S.

And this was really our first way of understanding what other types of data are out there that we can look at that doesn't have such a high percentage of missingness.

And so this was an area that we have been exploring. I'm running out of time, so I'm going to go through these slides really quickly. But as you can see, you know, here's some of the pediatric data that we have from the study.

The Enhanced Equity Research Hub, as mentioned a little bit earlier, and I really wish I had an extra slide or two here to show you the Enhanced Equity Research Hub, but you can search by -- this is all publicly available -- just Google Enhanced Equity Research Hub, you can search by race.

So for example, if you wanted to look

at the work that's been done in the space of the Asian population when it comes to clinical trial strategies, you would pull down here, and you would choose Asian.

The Enhanced Equity research aim, let's say you're looking at voices -- you wanted to understand what has been done to elevate and amplify the voices of our diverse communities, you would then scroll down here, and there will be a dropdown, and you would click Equity of Voices or Equity of Clinical Trials.

You'll be able to sort by age, so under 18, between 18 to 64, and above 64, ethnicity, and then disease/condition of interest.

We have not too many in here, but we have sorted it by, like, for example, sickle cell, hepatitis B, et cetera. This is a way for you to also sort by disease state.

And as mentioned, our newest initiative, the REACH consortium that was launched one year and three months ago.

So as we were growing the orange tree,

does anyone want to point out what was missing in the orange tree?

Michael, you want to try? No. Okay. All right.

So with the orange tree, the problem with the orange tree is that it takes about five years to grow an orange. And that to me is just too long of a time for us to recognize that there's a health equity problem and for us to take action.

So the Racial and Ethnic Minority Consortium, REACH -- remember I said, "acceleration," the A was important here, was a way for us to be responsive to health equity needs.

So here -- but we know, and, you know, Ms. Burgess brought this up, you can't be responsive if you don't have trust. If you don't have respect -- if you don't have bi-directional relationships, you will not have readiness.

That's just not how it works. I cannot ask a population to respond if there is no pre-existing relationship there.

So once again, it was developed for it to have a timely and efficient way for the FDA to connect with the diverse communities that we serve.

Here's some of the REACH consortium members. So they represent, for example, the federally qualified healthcare systems. In fact, we were just there the last month doing another town hall round table.

We have the University of Puerto Rico and the healthcare systems within Puerto Rico. We have the University of Hawaii and the Queens Medical Center within Hawaii. We have the tribal communities that will be presented by Dr. Billie Jo Kipp later on.

We have community centers, nonprofits, serving the Asian community, the LGBTQ plus community, rural communities throughout the nation, and we have our HBCU and faith-based organizations.

Here's some of our researchers. As you can see, they have a diverse background from physicians to HBCU presidents to tribal college leaders, from pharmacists to researchers, et cetera.

Some of the work -- I know I'm totally over time, so I won't go through all of this work, but much of the work that's being done in this space is actually looking at advancing clinical trial enrollment for diverse populations.

As mentioned, the next couple slides will just be couple pictures, but here's the FDA REACH panel that happened last April, which brought together our communities. Here's an example of the round tables at the agency. This was focused on rural communities.

And we also provide environments for our communities to connect, because as Ms. Burgess says, the humanization is so important.

So for the agency to have an ability to connect with the community leaders, with the HBCU presidents, with the tribal leaders, for that connection to happen and to foster and to create an environment for it.

And that's it. Any questions, which I'll take later on. Thank you.

MS. MULUGETA: Thank you so much, Christine. Our next speaker is Sue Rahman. She's the chief scientific officer at the Health Data Synthesis Institute.

Sue.

MS. RAHMAN: Thank you.

So as a pediatric researcher, I was invited to provide some insights from academia, but as a pediatric clinician, the voice of the patient is incredibly important to me. So the voice of children will feature throughout this presentation.

Now, this audience is well aware of the importance of pediatric clinical trials, but you may be less aware of their value outside of medical progress.

Years ago we spoke with children engaged in clinical research at our organization and asked them about their experiences, and we learned from them that clinical trials are a way for them to express their altruism; clinical trials allow them to engage with the healthcare system in a manner that may

be very different to what they experienced when they're sick, and in their own words, clinical trials offer, "Novel opportunities."

And it's my opinion and I'm guessing the opinion of almost everybody here, that those opportunities should be available to all children, irrespective of their circumstances.

More recently, we partnered with iCAN to understand children's perspectives on diversity in clinical trials. And the very first question I asked them was, "Is it important that research includes a diverse group of children?" And their affirmation was unanimous.

They spoke with us at length about issues related to equity and justice and inclusivity. But it was Ed who brought me to tears when he spoke about their importance to his psychological wellbeing.

(Audio plays.)

I don't feel alone. Have you heard a more powerful argument for inclusivity efforts in clinical trials?

We also asked the kids what they thought of when they heard the term "diversity" in the context of clinical trials. And not surprisingly, they identified age and race and gender and ethnicity at the top of their list.

But they also recognized a host of other individual patient factors that in their mind could contribute to the disposition and action of drugs.

So back to the topic of my presentation, which is the academic perspective, why is it relevant? This table here offers a snapshot in time at one point last year from clinicaltrials.gov.

There were 440 industry-funded studies posted to clinical trials that met the criteria listed there. And those 440 studies were enrolling children from 8,770 trial sites. And when duplicates were removed, 79 percent of those trial sites represented academic organizations.

So what this tells me is that the inclusivity behaviors adopted by academic researchers

shape the representation patterns we see in nearly all pediatric studies.

Apart from an investigator's own personal views on diversity and ensuring representation, can we identify other drivers that influence diversity in academic-led pediatric trials?

Well, legislation is one place to look. We have the NIH Revitalization Act of 1993, which assures that race and ethnicity is recorded for every trial that receives federal funding.

However, there's no enforcement mechanism in that legislation. Just because an investigator has to record and report racial and ethnic data doesn't mean they're ensuring representation in the trials they oversee.

Industry behaviors also influence diversity in academic-led pediatric trials. I've worked with industry sponsors for 25 years on trials and cannot recall a single point in time when I was asked about my experience engaging underserved populations.

When information was requested on demographics by way of feasibility questionnaires, it was often for the organization as a whole, rather than for the clinical trials we conduct.

So if representation metrics are lacking in industry trials, we may not be asking the right questions of clinical trial sites up front.

Industry also influences diversity in academic led pediatric trials through their enrollment strategies.

When a sponsor opts to engage a larger number of sites with fewer participants per site, you put investigators in a competitive enrollment situation, and that means they don't have the luxury of time or resources to engage less accessible populations.

And fewer resources mean less sustained investment in infrastructure for clinical trial sites, especially those trial sites that serve underrepresented populations.

So how are we doing in academia? We

chose to look at studies funded under the best Pharmaceuticals for Children's Act as just one indicator of representation in academic studies.

Across 34 studies, enrolling at 167 study sites, over 11,000 participants, we saw a reasonably strong agreement between observed enrollment and expected enrollment, based on census sampling at the same frequency in the same regions as in the clinical trials.

So big picture, it doesn't look bad, but if we restrict our view to this big picture, we are missing a piece of this puzzle.

When you start to break it down by geographic region, you can identify clear statistical trends of over and underrepresentation in clinical trials.

And when you break it down further by state -- in this example, I'm using an ecological marker of diversity as the metric, you can see a large degree of variability across the country.

I suspect that degree of variability

would be the same or magnified if we were able to look site by site. But those data aren't yet publicly available and I'm going to argue at the end of this presentation that they very much should be.

So let's go back to our kids. Why do they think some studies don't include a diverse group of children? And they had a lot of ideas. And I'm going to give you a second to look at those here, and we are going to dive into some of these in the next few slides.

One of the areas where we fall short in academic research is engaging participants with limited English proficiency. These data are from a survey we conducted of major research organizations across the U.S.

Now, what we were hoping to identify was the rate of consent form translation in these organizations. What we did identify was that 70 percent of the responding organizations were not able to pull this information from their IRB systems -- their own institutional IRB systems.

And if you can't review the data, you can't track progress or the lack thereof. When consent translation was occurring, it was typically into one other language and that was often Spanish.

Now, this issue was so important for us at my former organization that our IRB undertook a five -- a three year -- sorry, pilot study. What the IRB did was offset the cost of all consent translation for any federal or internally funded study.

And what we saw was an exponential increase year over year in the number of trials that had translated consent forms.

So progress, good, but we also recognize that consent translation is a very small piece of the puzzle of effective engagement strategies for non-native language speaking participants.

We also drop the ball when it comes to participants with limited literacy who may not fully understand the implications of participation.

And this can affect their interest in enrolling in the study. This can affect their ability

to effectively deliver on the requirements of a participant as laid out in the protocol. And this particular challenge requires solutions that are a bit more creative.

With funding from the National Endowment for the Arts, we chose to look at illustrated consent forms as one possible solution for this challenge.

We partnered with local artists and art students to create illustrations. We partnered with the community to vet those illustrations, and we worked very closely with the IRB to ensure that those illustrated consent forms met the requirements laid out by relevant regulations.

By the time I left that organization, we had illustrated consent forms in nine subspecialty programs at the organization.

We do a major disservice to our participants and, frankly, ourselves with the misconceptions we have about clinical trial participation.

The most misguided and damaging of which is that individuals of the racial and ethnic minorities are not interested in participating in research.

These are great data from Wendler, who demonstrate absolutely no evidence of decreased participation in interventional studies, in non-interventional studies, and in surgical studies.

But if you look at their data closely, what you will see is the minority populations are offered participation in clinical trials at a much lower rate than the majority.

I can corroborate the data from Wendler. I spent 25 years working with underrepresented populations, and whether we were doing cross-sectional studies, longitudinal studies, whole genome studies, our participation rates were exceedingly high. And that comes with effective engagement with the community.

We hamstring ourselves by designing clinical trials that are excessively burdensome to

participants and their families.

And this disproportionately impacts patients and participants of low socioeconomic status who may not have the bandwidth to accommodate disruptions to work or family obligations.

We went back and revisited those BPCA studies I mentioned earlier to try to understand how do burdensome elements get introduced into trials.

We looked at the elements that were introduced by sponsors. We looked at the elements that were recommended by regulators. And not surprisingly, both parties contribute to adding burdensome elements to protocols.

If we want to maintain an abroad population of patients, I recommend we start thinking about burden benefit considerations in the same way we've been taught to think about risk benefit considerations.

That means making sure we understand how children perceive burden as well. And we recently undertook a pilot in conjunction with iCAN to get at

some of that information.

These data from Kite underscore the importance of being thoughtful about what we ask patients and participants to do in clinical trials, especially when we think of the fact that many of the things we may ask them to do never translate into generalizable knowledge.

There are systems issues that hamper our ability to ensure representation in clinical trials. Organizational databases may not collect race and ethnicity data adequately, and they may actually collect it incorrectly.

This is a striking example of race and ethnicity data as reported by parents on a child's birth certificate versus what winds up in the electronic medical record. And look at the discordance for some of these populations. It really is quite striking.

But it's not just a system issue. If patients are reluctant to disclose this information, it may be because we're not asking the question in the

right way or we may not be explaining why this information is important to what we're doing.

Finally, there has to be an element of accountability, and academia has been doing a better job of making sure that metrics on race and ethnicity participation is made available.

This is not the forum to debate the benchmarking metrics that are being used. Needless to say, there are a number of them in that text box. They have their advantages and limitations.

But one, these are very big picture metrics, so they don't allow us to drill down. And two, the most striking thing, is that these are all retrospective. So if we want to impact representation in pediatric trials prospectively, we need different types of data.

We need to understand who is being provided care in academic organizations and how that compares to who's being offered clinical trial participation in those same organizations.

We proposed a metric that takes this

into consideration in a 2021 call-to-action paper that I had published.

And we encouraged, actually challenged, research organizations to make this data or similar data -- it doesn't have to be this metric, publicly available in the same way that we make outcomes data for interventional procedures like transplant and medical management, like cystic fibrosis, available site by site publicly for everyone to see.

A lovely example of where benchmarking can move the needle outside of the healthcare space is in the publishing space.

And these are some great data from the Cooperative Children's Book Center at the University of Wisconsin. They look at thousands of children's books every year, and they look at representation in those books and make that information available in creative communications like these.

And over the past 40 years, they've been integral in moving the needle on representation in children's books. And there is no reason we can't

do the same thing in pediatric clinical trials.

I am going to close by sharing what we asked of our children, which is, if you were in charge of research, what would you do to make sure studies were diverse? And they have a lot of ideas. We just have to listen.

A lot of the children we spoke to focused on communication and partnering and relationship building. But I will tell you, they astutely recognized that it's going to take an extraordinary effort.

These are some fun facts about the kids that I spoke to. And if you want to hear more from them in their own words, we've got excerpts from my interviews with them on the pediatric trials network.

But instead of my word, I want to close by giving the final word to one of our kids at iCAN, Rhiannon who when asked, "What would you tell researchers who think that ensuring diversity is too hard," responded with this:

(Audio plays.)

Thank you.

MS. MULUGETA: Thank you so much, Sue, for that great talk and for keeping us on track.

We're going to go ahead and take a 10-minute break, so if you can come back to this room at 10:30. So a 10-minute break, and come back at 10:30. Thank you.

(Off the record.)

PAM SIMPKINS: Thank you. Thank you very much, Lily.

Good morning, everybody. As Lily said, I'm Pam Simpkins, and I'm a managing partner at Mezzopointe. It's an R&D strategy consulting firm.

I've spent about 26 years in the biopharmaceutical industry. I just recently retired, but I have to say that the last 10 years were the most fulfilling, because it was 100 percent dedicated to pediatric product development.

So today I'm going to present a landscape overview of pediatric product development from industry's point of view.

Okay. So it's skipping some slides. Well, I'll speak to my disclaimer, which should be up there, but I have -- everything that I'm about to discuss today, the data and viewpoints are my own. I also have acknowledgements.

First and foremost, I want to thank all of the millions of pediatric patients and their caretakers, who participate in pediatric clinical trials.

The other acknowledgement, many things. I'm going to present a lot of data today. I have two data partners.

Oh, thank you.

My data partners -- as most people know in pediatric product development, a lot of data sets are not structured with pediatrics in mind -- there are many nuances, and so these partners have really helped me with evaluation very appropriately for pediatrics for 6 and 15 years respectively, so I want to give some thanks to both Maria and Sean [ph].

Okay. The slides are jumping around.

May I have some assistance with the slides? It should be agenda. Okay. Thank you very much.

So today, I'm going to cover four important topics, a historical view of industry-sponsored pediatric clinical trials, two short case studies that will bring the data to life, highlights of pediatric specific nuances, and a forward-looking view to set the stage for action planning.

Impetus. Okay. Thank you.

So why did I do this analysis, and why is it on the agenda? Well, there are many efforts underway to improve pediatric product development.

And I think all of those strategies would benefit from contextual information, such as who is conducting pediatric research; what diseases and indications are being studied; where are we going in the world to enroll patients; how long is it taking to bring innovation to children; what are the complexities, and where should we focus our efforts?

So I set out to answer those questions, because there are no pediatric-specific comprehensive

analyses of historical experience in upcoming trials.

I won't have a lot of time today, so I'm just going to focus on information that we can then use with a goal towards setting the context for knowledge expansion and strategy development, setting the stage for later sessions in today's meeting.

May I have the historical characterization? Oh, back. No, back from there. All right. Let's see.

Okay. Here we are. So let's start with the historical view.

So I reviewed 15 years of data, and I was focused only on industry-sponsored pediatric clinical trials. I included all phases, all indications, all countries, modalities, and sponsors.

And my resulting data set has 2,500 clinical trials all aiming to support the safe and effective use of therapies for children.

So what did I find? Who's conducting these studies? Approximately half are conducted by relatively large companies, and the other half by mid-

size companies and biotechs.

What percentages are required under the law? And some of this was alluded to earlier today. Two-thirds are required by the law, specifically the Pharmaceutical Research Equity Act or PREA, and one-third are voluntary.

And the voluntary ones are typically pediatric specific or pediatric-only studies, or they are conducted under the Best Pharmaceuticals for Children Act, or BPCA. And Dr. Heickman, later today, is going to talk more about the laws.

In terms of therapeutic area distribution, it wasn't surprising to me revealing dominance by immunology, inflammation, followed by neuroscience, and vaccines.

And the size and scope of our trials, excluding vaccines, shows small enrollment, which we expect, and significant dispersion across the world.

And I won't have time today, but there's so many other important characterizations to examine, and they will be worthwhile to review

certainly in other meetings.

Where are we going in the world? Over the 15-year period, the U.S. and the E.U. have been the primary locations for our pediatric trials, and I expect that to be the case going forward.

So I was very curious about what has been happening more recently. So in the last five years, I noted some noteworthy changes.

The war in Russia and Ukraine has halted research for children in those countries and in neighboring Turkey. China, South Korea, Argentina, and Canada have experienced significant increases in site openings, and South Africa and India have been declining significantly. Further investigation will be needed to understand why.

So let's put country enrollment in perspective. And Susan alluded a bit to this in terms of small enrollment per site. So let's dig in a little bit here.

So to provide a tangible example of what the last two slides really mean -- so small

studies with participants dispersed across the world, I'm going to share oncology.

Very low disease prevalence, total enrollment in late phases averages about 70 patients, and as you can see, we would need to go to seven countries to enroll, resulting in approximately ten patients per country. So this is a really good example of high dispersion.

In comparison, adult oncology trials are 15 times larger per country. So I highlight this. This is one of only many differences to consider as we craft solutions for children. Our strategies are fundamentally different than those in adult research.

So let's talk about time. How do all of these factors and many more that I could not cover today, including study design, contribute to the length of time it takes to complete a pediatric program?

An analysis done a few years ago shows that there is a nine-year gap -- nine years, between adult approval and pediatric data in a label. This

means that a new drug approved today for psoriasis in adults, as an example, might not have pediatric data until 2033.

During eight years of that time, pediatric programs are being conducted, and I think most people will agree this timeline is too long. And over the 15 year period when I looked over all my data, unfortunately, that average has not improved.

So as I said, eight years is the average across all indications. But if you drill down to timeline estimates at the indication level, you'll see that each indication varies.

So the starting point for ulcerative colitis, as an example, might be nine years, but landscape dynamics will impact this time.

What do I mean when I say, "dynamics"? Let's look at UC a little bit more closely. But first some context.

UC does occur in children, mostly in adolescents. It's more aggressive in children than in adults. So we do have a sense of urgency. There are

approximately 2,000 children in the U.S. with moderate to severe UC.

There are no differences in phenotypic presentation that have been noted by race. However, differences in clinical outcomes have been noted by race. Therefore, much more work has to be done. This will require a much better understanding of the science and of social determinants of health.

Given this context, let's say a sponsor plans to complete a program in nine years. But that plan must be executed at the same time that several other products are trying to enroll the same participants. In moderate to severe UC, there simply aren't enough children to enroll them in all of these trials.

So let's take this example. On the left-hand side you see that there are 16 trials currently enrolling or planning to enroll in moderate to severe UC during the 2024 to 2030 period. These are actual studies.

On the right-hand side, some data

points. As I mentioned, there are only 2,000 children in the U.S. with moderate to severe UC. 415 of those children, or 20 percent, are currently being prescribed at least one newer drug off-label. So those children will not participate in a trial.

Sixteen concurrent trials are active or will be as I mentioned. And so given this situation, it will take 20 years to complete all of these studies, not 9.

So I present this example, because in pediatrics, adding in market dynamics and other factors specific to the indication and to the children who suffer from this disease, is absolutely critical. When you do that, the nine-year timeline is clearly unrealistic.

Let's switch to an indication with higher prevalence and see how historical data can be used to inform a strategy.

So asthma is a good example. We know a lot more about the presentation in children by race and by gender. We also know where the asthma capitals

are. These are cities with the highest prevalence, highest ER visits, and highest deaths from asthma.

So I mapped those 20 asthma capitals shown here, and I also mapped historical patterns of site activations. In doing so, I identified a sponsor that was very consistent in site activations in those asthma capitals. So I contacted them.

I interviewed a leader at that company and received their permission to present this blinded case study.

I learned that this sponsor did not face the magnitude of concurrent trials, like my UC example, but they faced other obstacles, and some of those we've covered early this morning.

Distrust of research among parents, grandparents, faith-based leaders, and children was a significant issue.

In addition, social determinants of health factors like environmental, air quality, living with grandparents, reliance on adults for transportation, use of electronic diaries, all became

major considerations in the enrollment and the retention strategy.

And so my takeaways from this great interview were these: Go to where the patients are; reduce their burden; know the location, and understand the needs of diverse participants by going into the communities and asking; put a patient-centered strategy to work; community programming around working with school nurses was quite pivotal for this leader; add adolescents to adult trials to drive faster access, and use data science, specifically extrapolation, which is the borrowing of data from other cohorts, either adults or older children whenever that's appropriate.

All of these things in this leader's mind were absolutely critical to shortening the timelines.

With this in place, the leader's goal was to cut the median timeline almost in half and collect generalizable data, because her participants would reflect the population intended for this

therapy.

And while she's not quite done with the trial yet, she fully expects that this strategy will help her team collect all the data that they need and exceed their diversity goal. It was a great story, and it was wonderful interviewing her.

So at a much higher level, this historical landscape work enables us to narrow our focus on important actions that can have a positive impact on the quality, speed, and efficiency of pediatric product development.

It also deepens our understanding of the challenges, all of which I'm confident we can overcome so that we can be proactive and thoughtful in addressing them. And I only list a few here.

So let's wrap up the historical view. Pediatric product development continues to be long and complex, and I hope the data and examples I provided gives you perspective on what I really mean when I say that.

Given our collective goal to improve

the process and outcomes for children, I hope this historical perspective provides good context for forward-looking strategies, including those needed to achieve the appropriate representation in our trials.

So with history behind us, let's look forward. How do we know what's coming down the pipeline for pediatrics? Well, what we do, typically, is we look at the adult pipeline.

Why? You'll remember earlier I mentioned that 67 percent of pediatric clinical trials are required under PREA, and, therefore, they typically follow the adult approvals.

So the adult pipeline is often used to provide directional feel for upcoming industry-sponsored pediatric clinical trial activity.

So I looked at the adult pipeline. This slide shows the volume of late stage adult clinical trials currently happening in these six indications.

I pulled these six, because they are very relevant for pediatric research. If the products

in these indications are approved, it is very likely that a pediatric clinical trial will be required by law.

Based on this volume, it's likely that we will have some challenges with multiple concurrent studies in type-2 diabetes, obesity, and atopic derm, very similar to my UC case study, since many companies are pursuing new products in these indications.

So my question is, given what we know about these indications and about historical patterns discussed today, what insights can we apply to future pediatric trials? How can we be proactive?

Wrapping up, we know what's coming. Significant upcoming pediatric activity will be important in ten plus indications, and we have the opportunity now to plan to do better -- better in trial designs, better in enrollment, better in achieving diversity, better in creating faster access for our children.

What I do know is that we can do it together, and I love when Michelle said, "Endurance

for hope." I have very strong hope that we can do it together.

I'd like us to use this information and our collective knowledge to formulate actionable strategies that benefit all children, so they have speedy access to the therapies they deserve.

Thank you so much.

MS. MULUGETA: Thank you so much, Pam.

We're going to transition to the panel discussion now, and I would like to invite Dr. Dionna Green, who is the director of the Office of Pediatric Therapeutics, as well as Lois Lee, who is a senior associate in Pediatrics in the Division of Emergency Medicine at Boston Children's Hospital, to co-moderate the panel discussion, along with the panelists, if you can go ahead and come up now, please.

MS. GREEN: Well, thank you to all the panelists today who have already spoken, and then we have three panelists who are joining, and we have questions from our virtual audience, but also we would love to take questions from all of you.

But we are going to start with our three panelists who have not presented yet. And first is Sneha Dave.

If you want to, just tell us a little bit about why you're here today.

MS. DAVE: Yeah. Hi everyone. My name is Sneha. I am the executive director at Generation Patient, which is an organization I created when I was 13 years old.

I've been living with severe ulcerative colitis since I was a little under 6 years old. And I had the colectomy surgery, which is the removal of my large intestine, when I was in high school, which prompted me to create one of the only organizations focused on young adults, so thinking about this transition period between pediatric and adulthood.

And now, we have four staff members. We're entirely young adult patient led, and we focus on areas of peer support, health policy, which includes clinical trials, and leadership programming.

MS. L. LEE: Thank you, Sneha, for

joining us today. So we're just going to start with a few questions for you.

Given Dr. Abdel-Rahman's presentation included -- I love the videos with the input from our patients regarding their thoughts about clinical trial diversity, what stood out to you about some of the perspectives they shared?

MS. DAVE: Yeah, I think the last video with Rhiannon was particularly empowering for me personally, and I think really alludes to the point that there's an urgency that we, as patients, feel that may not always be felt by those who don't have the same lived experience of being a patient.

I also think, in general, from the presentation and from the perspectives, it was really fascinating, because I think we think about engagement and about community as part of the trials, and I think maybe 80 percent of the conversations that were being had or problems can be solved by engaging the community members.

But I even think it goes beyond

engagement and thinking about how can we have patients leading as PIs on some of these projects and some of these clinical trials.

I think, you know, we especially as young adult patients, see our role as not only engaging, but also being able to drive some of this research.

So for example, on a PCORI award, which is not a clinical trial, we are the youngest PIs on a PCORI award. And so really thinking, you know, differently about how we can be engaging and enabling patients to be driving some of these outcome's endpoint developments from the very beginning I think was really -- yeah, pardon my perspective.

I have other things but I'll pause, because I don't want to take up the whole panel.

MS. L. LEE: Do we have any questions for the audience? Otherwise, I'll have one more question for Sneha.

Okay. One more question for you. As a patient representative, what are some of your key

concerns about trial participation that differ across diverse pediatric populations?

MS. DAVE: Yeah, I think, for myself -- so my parents are both immigrants from India, and so thinking about the different cultural backgrounds of how western medicine has been viewed and really being able to open up conversations about, you know, what are your beliefs as part of this trial, in addition to these standardized therapies that we're thinking about.

I also think in terms of being able to communicate things in a plain language, you know, like, "We're testing this for this reason," is the way that you could just make things very clear and simple in terms of communicating what a trial is in the first place, because even the word "clinical trial" feels very scary to a lot of people, especially for kids and younger folks.

And then just two other things really quickly on that. I just really feel like there's a huge opportunity with long-term safety data and a lot

of questions that we still think about as patients, but also I can only imagine for care partners and parents what that's like.

And I think there's a huge opportunity to do a better job with being able to show that this is how we're going to be thinking about long-term safety data after the trial. And, I mean, I know in IVD, there's so much that needs to be done.

So anyway, last thing I'll just say is the affordability of the therapeutics, especially as we're aging into adulthood, older adolescents, I mean, we are thinking about the financial repercussions of being able to afford therapeutics after the trial as well.

So post-trial access is something that needs to be clarified, because, I mean, personally, I'm on a medication that costs a lot of money, and I have to make decisions about my life based off of that.

And so when we're thinking about trust, I think, you know, part of that is are we making sure

that these therapeutics are available and accessible and affordable after the trial too.

MS. L. LEE: Thank you very much, Sneha.

So next I'd like to turn to you, Dr. Bourgeois, to introduce yourself, and then we have a couple of questions for you.

MS. BOURGEOIS: Wonderful. Hello, everyone. So nice to be here today. My name is Florence Bourgeois. I'm a clinician scientist at Boston Children's Hospital and Harvard Medical School.

My research focus is around building informatics-based tools to support pediatric infrastructures or research infrastructures and clinical trial networks and evaluating methods and new approaches around policies and statistical tools to conduct research towards the development and approval of pediatric therapeutics.

MS. L. LEE: Great. Thank you very much. So we just heard from Pam Simpkins, and she really did walk us through a very in-depth pediatric

landscape analysis that was rich in data and had quite a few insights that I think will be food for thought for all of us to chew on throughout the rest of the day.

But I'd like to start with you to first hear what are some of your thoughts on the information she shared?

MS. BOURGEOIS: Yes, thank you for that. So I think Pam's presentation was really terrific and pivoted a little bit from the issue of diversity in clinical trials to the more fundamental question of just equity for kids period compared to adult drug development.

So a lot of the data that she showed, again, underscored the need to highlight pediatric research and drug and device development for children, because the focus continues to be for adults.

I like to say that most drugs and devices are not developed for children, but they are sometimes eventually studied in children.

And so this driver of the adult

priorities then being sort of what we end up with for kids is something that we should really think about, and what are some of the approaches to pivot towards a focus that is driven from the pediatric-needs standpoint.

MS. L. LEE: And so based on your experience, given your research and looking at participation in diversity, where are some areas that you feel that things are going well in terms of diversity in clinical trials?

MS. BOURGEOIS: Yeah, that's a good question. So with drugs and devices in particular, many of these trials are for diseases that are primarily treated in tertiary care organizations -- the hospitals, which tend to be in more urban locations.

And so for drugs and device trials we tend to see greater diversity, which was actually nicely shown in the study that I think Christine maybe showed where the -- or no, Sue, with the BPCA studies and their representation.

So among drug trials there was good representation and diversity for those studies. Again, these are very specialized interventions in patient populations, so we're doing well on that front.

But as you pointed out, this may not generalize to all trials across other types of diseases or intervention types.

MS. L. LEE: Thank you. And do we have any questions from the audience before we move on to our next panelist?

Well, I invite you to think of your questions and please just line up at the mics, and we will call on you once you do. Thank you.

MS. GREEN: Next on our panel is Dr. Ann McMahon. So if you could, tell us a little bit about why you're here today and we'll have some questions for you as well.

MS. MCMAHON: Thank you. My name is Ann McMahon, and I work at the FDA. I've been here for 22 years. And I think that you heard Dr. Lee talk

briefly about the study that they are funding for us to do in the Office of Pediatric Therapeutics that we've been doing over the last year. And so I wanted to just say a few words about that.

I just also wanted to give credit to the team, which has been working on this, from the Division of Pediatric and Maternal Health and from the Office of Pediatric Therapeutics and from the Office of Biostatistics.

We looked at trials submitted to the FDA under BPCA and PREA and focused on children with diabetes type-1, diabetes type-2, and obesity.

We chose those diseases, because there are high proportions of Hispanics and non-whites among children with these diseases in the U.S. Therefore, potential underrepresentation of these groups could have an important effect on the population at large.

We used three U.S. databases giving us races and ethnicities in the general population of children with these diseases in the U.S., the Search study for Diabetes in Youth, the National Health and

Nutrition Examination Survey, or NHANES that you may have heard of, and the U.S. Census data.

We performed chi-squares to compare clinical trial, race, and ethnicity prevalence in the general population with the -- sorry, the clinical trial race and ethnicity prevalence with the background data that is the disease-specific background data and the prevalence of race and ethnic ethnicity in that.

So what we found, the preliminary data is that compared to the race ethnicity distribution in the U.S. pediatric population with diabetes type-1, type-2, and obesity, there was strong evidence of underrepresentation at the P less than 0.05 level by race and ethnicity for diabetes type-1, diabetes type-2, and obesity.

Yeah. That I can -- I'm not going to go into the specific numbers. We're putting together our data at the moment, but it's definite that there was underrepresentation in a number of the trials submitted to the FDA.

MS. GREEN: So it's great to hear about the internal work that's being done at the FDA, as well as we heard about some of the external work being done in academia and industries.

So obviously, having everybody's sort of eyes on this, you know, moving forward will help us improve our enrollment and participation.

We had sort of talked about some metrics for appropriateness for the prevalence of race and ethnicity in pediatric clinical trials. So are there any existing, you know, metrics that we can kind of look to as we build metrics for the future?

MS. MCMAHON: Well, our study gives you an example of a quote metric, which is P less than 0.05, comparing to some background group as compared to the clinical trial.

But I would not say that that's, by any stretch of the imagination, a metric that has been accepted in the general research community.

And I would say that my search of the literature suggests that various statistical methods

are generally used to determine underrepresentation, but I didn't find a lot of concurrence about specific statistical methods that should, quote/unquote, be used.

MS. GREEN: Thank you. And I think part of the problem has also been pointed out; we don't know the true prevalence of the diseases in some of our population, so it's hard to know what the baseline is, much less where we should be as far as our enrollment. So thank you.

MS. MCMAHON: Thank you.

MS. L. LEE: So Ann, there was one clarifying question for you online, which was what data sets were used for the pediatric study that you're describing? Can you clarify that those studies were submitted to the agency and maybe just talk a little bit more about that.

MS. MCMAHON: Sure. The studies that we used were submitted under BPCA or PREA, and I can't tell you which studies were for which right now, but they were submitted to the agency under BPCA and PREA.

Carla, do you want to say more? Okay. Yeah.

MS. L. LEE: Okay. Thank you very much. And we have a question from the audience. Please, go ahead, and if you can, say your name, affiliation, and your question.

MS. EPPS: Okay. Thank you. Good morning, everybody. My name is Carla Epps. I'm from FDA from the Division of Pediatrics and Maternal Health.

My question is about, for me anyways, an elephant in the room that some people don't apparently see, which is the fierce urgency of now -- in addressing diversity in the pediatric population.

I was actually one of the members of the team that Ann alluded to and for some other of my work.

What I wanted to point out is that for the pediatric population in the U.S., it is already a minority majority population, and yet I don't hear how that's being taken into consideration for activities around this issue. So I don't know if people wanted

to speak to that.

Thank you.

MS. L. LEE: Would anyone like to start? Do you need a clarification? I think there needs to be a little clarification on the question.

MS. EPPS: I guess one is just, do you hear in activities that you all are involved in about the fact that our children are a very diverse population, more so than the adults, and what does that -- already, and rapidly increasing, and what does that mean in terms of the pace or the focus of activities on increasing diversity in pediatric trials?

Thank you.

UNIDENTIFIED SPEAKER 1: I don't know if this answers the question exactly, but what I can comment on is the need to capture that diversity more accurately.

So right now, when we're making comparisons between diversity in clinical trials and the U.S. population, we're largely using U.S. Census

data, which if you look at it, is quite crude and really not reflective of the current demographic diversity in our children.

For example, there's an increasing proportion of children who self-identify as multi-race or ethnicity. And that is not accurately captured, neither are many of the other emerging subgroups.

So I would say in order to adequately address this moving forward, we also need standardized race and ethnicity classifications that reflect our pediatric population.

MS. C. LEE: I just wanted to add to that. That's a great point. So currently right now with our OMB SPD 15, there is an update to our standardization of race and ethnicity capture. So right now, patients can check more than one box.

So for example, my son can check Asian and white, as my husband is white. So this will increase our availability of data standards, but going -- sorry, availability of data.

But going back to Carla's question, as

she's asking the question, I keep thinking back to the last round table that we had, which was in the rural communities.

And as we know there is a very high increasing proportion of diverse children in rural communities, and there's, you know, very unique nuances and barriers that we need to increase our awareness to.

So thank you so much, Carla, for that question.

MS. L. LEE: Thank you. So we're going to take one question from online, and actually it has to do with Michael being willing to share earlier, and again thank you Michael, your struggle with having to wait four years to be in a clinical trial.

And so the question is, the individual states that this reminded them about the gap that exists, that Pam pointed out between when a product is approved for use in adults to when there's information for use in children in the labeling.

And their question for the full panel

is, do you think that diversity action plans will help shorten that gap, or do you think it will become yet another barrier to the prevention of efficient and effective pediatric clinical trials?

MS. SIMPKINS: I'd love to start. So as my data showed, we really have to look indication by indication. So I don't want us to make sort of broad sweeping commentary about like all of pediatric product development, because I think that would be a disservice.

The last thing I think we want is to add to the number of years. That gap can grow if we make sort of blanket statements or goals about what we ought to achieve.

I'll just draw on the example from the ESMA interview. What I found was really striking with this particular leader. The reason she was so confident that she could cut the time was because she was very focused on excellence by design.

So at the very beginning of your design, as you're crafting your strategy, you know

that diversity has to be very critical to your success.

We all want generalizable data. You can't have generalizable data if your data doesn't reflect the population intended for treatment. So that's a tenant that we've always lived by.

So start with that as your design at the very beginning, and I'm confident then that actually you will shorten the timeline, because you're looking at the right population that ought to be enrolled.

MS. L. LEE: Thank you. That's a great point. Anyone else? I think that summarizes it, because yes, being intentional from the outset, being strategic, and also leveraging best practices, which we hope will come out of a workshop like today, that will help inform other investigators and sponsors about what has worked and what clearly doesn't work, is going to help us move forward.

So next we'll go to a question from our audience.

MS. MCMURRY-HEATH: Hello, Michelle McMurray-Heath from BioTechquity Clinical. We're a CRO helping companies diversify trials. And I just wanted to expand upon the earlier audience question, which is something I hear a lot from pharmaceutical companies, what does good look like?

We know what bad looks like, but what is the goal? Is the goal representation of the general population? Is the goal representation of the diagnosis? Is the goal just enough representation to get statistically significant conclusions?

I think we need a conversation about where we're trying to go, so everyone can, you know, adjust accordingly.

MS. L. LEE: Very fair points. Thank you very much.

Yes, please, Ann.

MS. MCMAHON: That's a great question. And you know, we debated it some, but pretty rapidly came to the conclusion that we thought it was fair to compare clinical trial -- the disease or condition

that was being studied in the clinical trial, to compare that to that disease or condition in the general population.

And in this case it's the general population in the United States, because FDA was the one that was receiving the information.

So that's where we came from. I think it's fair, but I know it's not the only possible answer.

UNIDENTIFIED SPEAKER 2: One additional thought on that is beyond thinking about sort of the necessity of having generalizable results through good representation, I think another factor to consider is also good needs to mean that we have equity in terms of access to new innovative emerging therapies across diverse populations.

So it's not just about generalizability, but it's also about equity to access to these therapeutics.

MS. GREEN: One more question from our audience, and then we'll take a question from the

virtual audience.

MS. KIPP: Thank you for that question, and I wanted to follow up by what is good. And so I think it's -- I am trying to struggle with this, because what is good for one community might not be good for another community, because there are historical difficulties with the medical model with certain communities, and certain communities have struggled and victims been victims of poor research and poor medical research science.

So what would good be like in communities? Would that be maybe the community saying -- because I think we're looking for a gold standard of good, and I don't know if that's the answer.

I think communities with the researcher with outcomes with clinical trials define what is good for them.

MS. C. LEE: Thank you so much, Dr. Kipp. You're always here with so much wisdom. That is entirely correct. In fact, what we have seen is

that beyond just the communities themselves, it also depends on the disease state.

For example, our work with the Hepatitis B Foundation, what we have found is that religious leaders are a no-go when it comes to clinical trial diversity.

So many times with stigmatized conditions, having religious leaders convey the clinical trial message actually prevents the community from engaging in clinical trials.

So beyond just race and ethnicity, I think it's very important to look at the disease also. Also, working with the tribal nations, gene therapy has many layers of, you know, I think, nuances before we even get to the conversations when it comes to gene therapy.

Another issue that I wanted to highlight from Dr. Kipp's point is that if we are not careful with engagement, many times what we have found is that the community will close its doors to us.

So you know, that is something, and it

is almost impossible to reengage then, and you might have to wait generations for that next opportunity.

So just for something to think about beyond race, ethnicity, age, geographical location, disease states, the nuances are incredibly important to understand.

MS. GREEN: Thank you. So we're going to take one question from our virtual audience and then one more question in the audience here.

So this is for Dr. Christine Lee. Many clinical trials are global as we've seen today, and in these countries race and ethnicity information is not even disclosed due to privacy concerns -- although, only aggregated data are usually what's reported out, is the FDA collaborating with other health authorities in other countries on this issue?

MS. C. LEE: That's a great question. Did this person read my mind? Yes, that is a topic that we are currently exploring in great depths, and we hope to, you know, have something out in the next year or so. So yes. So, you know, I guess they did a

spoiler. Oh, yeah.

MS. GREEN: Okay. And another question from our in-person audience.

MS. HILDEBRAND: Yeah. No. Thank you for allowing me to ask the question. And great discussion so far, and I would, I think, have two points intertwined, which is a little bit started, Pam, by your great presentation on the history of things.

I'm not a hundred percent sure that the future will really look the same, and we embark so much on PREA and adult indications. If we look in the upcoming -- what is coming in the science on cell and gene on the high medical need and ultra-rare and rare diseases, which for me pose two questions.

I think we may see a much higher need for education for patients and doctors with regard to this, because treatment pathways will even become much more complicated.

And on the other hand, studies may become much smaller on the one end, but on the other

hand we may really need much more global reach for this.

So I think for me it's a question, how can we go in with a diversity paradigm, which focuses and only on the "prevailings" in one country, because I think we -- we really have then to look global and -- if we look in rare diseases, ultra-rare diseases, cell, and gene.

So that might be the next iteration, because this is a great start point, but I really wonder what would be the outlook for this.

And it's for the whole panel. I don't know who starts.

MS. SIMPKINS: Well, I'll start. So as you can fully appreciate in my dataset, there was so much that I could not cover today, but I did see real momentum in cell and gene therapy, and the fact that children -- because many -- you know, these are congenital diseases, you're seeing children enrolled in first-in-human studies; right?

So that's going to -- I think that's

going to change what we've seen historically with that pattern of children following adults.

There's a merge now here between what I think we've been learning in the rare disease community and pediatrics.

I mean, you know, you could argue that all pediatric or most pediatric diseases are rare diseases, but I think historically we haven't really talked about them together. But here, we're seeing sort of a natural merge where we can share strategies, learn from each other.

But I do think it's going to be a very different paradigm, because we're going to see studies where the first label will include children, at least the cohort of children.

MS. L. LEE: Anyone else? Okay. Well, then I would like to turn to youth too, and I want to thank you for your presentation.

I think your incorporation of the patient perspective was very powerful, and I had the chance to look at some of the other parts of your

interview by going to the link you mentioned, and I hope the rest of the audience will as well, because there's some really important pearls of wisdom that these children are providing to all of us.

But my question for you is, based on all you know and all of your experience, where can a investments be made that's going to really help to enhance representation within clinical trials?

MS. YAO: I think there are a lot of areas and many of which I touched on in the talk, and I want to kind of leap off from the point you made about these intentional designs when it comes to trials.

And we can have the best intention when it comes to intentional trial design, but if your academic partners can't deliver on providing the patients, that's a real problem.

And I firmly believe that there should be some benchmarking mechanism that is available. We have to be able to -- if I've got a rare disease and I've got the luxury of resources, I'm going to look

for the hospital that's got the best record for outcomes for that disease.

And I think industry should be able to look at data preemptively to make intelligent decisions about clinical trial site selection. So I certainly think that's one area.

Another area where investments are probably sorely needed, and I think we heard kind of that reinforced through a lot of the presentations today is in educational toolkits, education around communication, and toolkits around communication.

We cannot approach partners and their parents, communities, children, for research in the same way we approach them for clinical trials -- I mean, for practice. You know, my communication with a patient is very different when I'm caring for them.

It's a lot more paternalistic and informative, as opposed to when I'm trying to engage them in clinical research. Which again, we've heard that term "bi-directional" a lot; it's very bi-directional.

It involves a lot more listening than it does communication. And I don't know that we are taught that as we as investigators. I think it's something that we either -- is innately a part of what we do as clinical academics and practitioners or it's not. And I think there needs to be some guidance there.

MS. L. LEE: Well, we're very fortunate to have a representative on our panel from Generation Patient, and we would love to hear your thoughts about communication.

What are areas where you see that there's maybe training or input that we can all take away to say how best can we communicate to patients and families about the importance of clinical trials, but also ensuring we're listening clearly to their needs?

MS. DAVE: Yeah, definitely. I think one thing that's always been really tricky for me to understand is the wide developmental stages of pediatrics. So thinking about the fact that, like, a

8-year-old is very different than a 16-year-old, and the materials needed to be delivered to a 16-year-old might not look like cartoons or things that are, like, you know, more for younger children.

So I think it's really important to, one, note that, but two, it's really can be confusing sometimes when care partners who have the best intentions are also in the mix.

I think sometimes, you know, parents tend to -- with all due respect to my parents, you know, tend to, you know, think that they know what's best for their kids, and they certainly are trying their very best.

But at the same time we need to ask kids even if they're 8 years old, 9 years old, we need to give them that agency and that power that they can, you know, make informed decisions or be part of that process.

And I think this generation of kids that are coming up are going to have the tools to be able to do that more so than any other generation of

kids.

And so I think we can utilize social media, graphics, and things like that, and I really do think there's an opportunity for the FDA to even work with more community groups to develop more plain-language materials for their communities.

And even education that the FDA is putting out, I think can be designed by community groups for the broader public as well. So yeah.

MS. GREEN: Thank you for that perspective.

So in our last few minutes, trying to end a little bit on a high note, what is already being done that is successful that we can continue and should build upon? And this is open to all our panelists.

MS. SIMPKINS: Okay. I'll jump in. So something I'm really excited about, specifically in pediatrics, is the use of data science. There's so much that we already know and we should be leveraging that data to supplement what we could learn in

clinical trials.

Almost to the point where in many instances our trials don't have to be as long and as big as they are, because we're borrowing data that already exists that can really inform the safe and effective use of our therapies.

I'm thinking specifically of extrapolation -- I'd love to see a stronger uptake there, and really public/private conversations around the use of extrapolation, because I think there's a lot that we can learn from each other, other types of data science techniques, like the use of Bayesian statistics. There are a number of different things that we can do with technology and data to really streamline pediatric product development.

If you can't tell already, I continue to be disturbed by the length of time. I do think that we have a lot at our disposal to help bring medicines to children faster.

MS. YAO: I would say an area that I'm very excited about is the emergence of remote clinical

trial participation. Accessing populations who, you know, Michelle mentioned you're seven miles from Lurie, but seven miles in Chicago takes 40 minutes to get there.

So making sure that we are starting to look at trial designs that allow us to go where the patient is instead of having them come to us.

UNIDENTIFIED SPEAKER 3: I'll expand just a little bit on the sort of potential of data science that Pam brought up.

So in addition to extrapolation, there are vast amounts of digital data now available that can be accessed to augment and complement randomized controlled trials, which as we know are incredibly resource intensive and difficult in small dispersed populations such as many pediatric illnesses.

So with all these electronic health record data, for example, insurance claims data, we can conduct observational studies, again to complement our traditional RCTs.

The big issue there that remains to be

addressed is that beyond just demographic factors, what we really need are many of the variables that get at social determinants of health. And that is currently incredibly challenging.

And so thinking of ways that we can better use these observational data sets to capture these relevant variables to get at differential access to healthcare and responses to different types of interventions will be a critical step to make full use of this potential additional resource.

MS. MCMAHON: We're providing -- at the moment, working on a article talking about pharmaco epidemiology in pediatrics, and one of the things that we're talking about is putting AI in there, and I would say AI is something that is probably going to make a difference in the coming 10 to 20 years for -- exactly as you were saying, for pharmaco epidemiology in pediatrics and in general.

And also, I just wanted to say that this kind of a conference that that is being put on today is a great boon for the field. I mean, I think

it really gives us a sense of where we need to be going.

MS. L. LEE: Excellent. Well, thank you. I think you'll have the last word there, Ann, because we're at time, and I think that's a really nice way to summarize it.

This conference is signaling where we're going, but it's also signaling what we're prioritizing.

So I want to thank our panelists and speakers for their input this morning and expertise. Please, join me in thanking them.

MS. MULUGETA: Thank you so much. Thank you to our moderators and panelists. This marks the end of Session 1, which was Current Status of Pediatric Trial Participation and Lessons Learned.

So the rest of the day we'll focus on inclusion strategies. So we're going to go ahead and take a one hour lunch break. So if we can reconvene at 12:30. That's slightly less than an hour, but 12:30 if you can please come back so we can get

started with the rest of the day.

Thanks so much.

(Off the record.)

MS. MULUGETA: We're going to go ahead and get started.

So we're going to go ahead and get started so we can stay on time. So we're going to start Session 2 with some case examples of inclusive trial designs.

Our first speaker is Rachel Randell. She's an assistant professor of pediatrics at Duke University and Duke Clinical Research Institute.

Rachel.

MS. RANDELL: All right. Thank you. And thank you all for being here this afternoon. This morning's content mentioned a couple times, decentralized or remote trials, so I'm very excited to share with you an example of one of these types of trials.

At the Duke Clinical Research Institute, we like to call these types of trials --

sorry, I'm having some difficulty with the clicker here.

Well, I'll just say briefly that at the Duke Clinical Research Institute, we like to call this type of trial "Direct to family" to highlight the critical importance of the family in pediatric trial participation.

Thank you.

And that includes of course, the primary caregivers, but also the greater family, the community.

So these are our funding and disclosures. So I think this group is very well aware that pediatric trials are difficult to conduct for many reasons. However, multicenter research networks have been able to overcome these many challenges to successfully conduct trials in children.

One example is the NIH-funded Pediatric Trials Network, or PTN, which has over 200 sites, to date has conducted more than 50 studies, and data from those studies have led to 21 FDA label changes to add

pediatric specific information on therapeutic dosing, pharmacokinetics, and safety.

Another example that's specific to my field of pediatric rheumatology is the Childhood Arthritis and Rheumatology Research Alliance or CARA Registry.

So for those who aren't familiar with the structure of a multicenter research network, I've provided CARA here as an example.

So the map on the bottom left-hand corner of the slide, you can see in blue and teal circles, these indicate sites, which are individual children's hospitals or clinics where families and children go to receive their clinical care for their rheumatologic condition and also participate in research.

These sites then report to a central site, a coordinating site, which is the Duke Clinical Research Institute actually for both of these examples.

And then depending on the structure of

the research network, there may also be a separate data coordinating center. So one can imagine that this gets incredibly complicated. It's also expensive and slow.

The operational overhead for one of these types of trials is estimated to be about $10,000 and 200 hours per subject enrolled.

On this slide, I was planning to discuss some of the potential barriers from the family's perspective. But I think after today's KEYNOTE address and such a wonderful journey that Michael shared and Michelle's talk, there's absolutely nothing more I need to say about that.

Instead, I'd like to share with you an approach called "Decentralized trials," also referred to sometimes as "virtual remote" or "direct-to-family," or "direct-to-participant" trials.

So instead of asking the family to travel to a research site, which then reports to a central site, we basically flip that on its head, and we, as the central site, work directly with families.

There are lots of examples of different types of studies that have been done this way, but really a key underpinning is the use of technology for remote data collection.

This occurs through things like video conferencing, devices, wearables, as well as electronic questionnaires that can be completed on a cell phone, tablet, or a computer.

It's also possible to obtain biological samples in this type of study. For example, you could have a home health phlebotomist to travel to the family's home to do a blood draw.

You could also ask them to travel not to the research site, but to a local commercial laboratory for a lab draw. And it's also possible to self-collect a variety of biospecimens, including blood.

So at the DCRI, we were curious to know could a direct-to-family design overcome potential barriers to pediatric trial participation? And we thought, well, maybe.

We could schedule these visits flexibly on evenings and weekends outside of typical work and school hours. We could deliver study materials and study personnel directly to the family's home to eliminate transportation barriers.

Maybe this could reduce some of the financial burdens. And we also felt that we would be free from the geographical limitations placed by sites.

So this inspired the Individual Patient Exposure and Response in Pediatric Lupus or iPERSONAL trial. This was a direct-to-family open label, proposed pilot trial evaluating the preliminary effectiveness of a medication management device on adherence to hydroxychloroquine in pediatric systemic lupus erythema ptosis.

Okay. That was a really long statement. I think I had to take four breaths in the middle of it. So let me break this down for everybody.

Lupus is a rare chronic autoimmune

disease that disproportionately affects women and women from these racial and ethnic groups.

It unfortunately is a leading cause of death in young women. Diagnosis during childhood is common and predicts a worse prognosis.

Now, the good news is there are safe and effective therapeutics. One of them is hydroxychloroquine, which is a once daily oral anti-malarial medication that's prescribed to almost everyone with lupus, although like with many other chronic conditions, actually taking that medication every day as prescribed is a major challenge.

So we saw this as an opportunity to potentially improve lupus health outcomes by promoting adherence to this medication already prescribed as standard of care.

And we thought this direct-to-family design would be especially important for lupus, one because of geography. So lupus is rare. Rheumatologists are rare. Pediatric rheumatologists are especially rare.

So reducing barriers in terms of transportation we felt was very important. We also know that socioeconomic and other factors that present barriers to research participation also negatively affect lupus health outcomes, and with a lot of other conditions, there is a major issue with racial and ethnic diversity historically in lupus clinical trials.

This next slide illustrates basically our study activities. So the intervention was this electronic pill bottle with a sensor in the cap to record bottle openings and closings.

It also provided automated reminders, so flashing light, a chime, and automated texts and phone calls around the time that medication was due.

All participants received the intervention and were instructed to use it for their hydroxychloroquine that was prescribed and managed by their doctor.

After a two week run-in period, we activated reminders, and they remained active for the

duration of the six-month study.

So throughout this time we had four in-home visits where a home health nurse traveled to the family's home to collect a blood and urine sample, help the family submit data using their devices, and complete questionnaires.

At the first visit, we also had the home health nurse connect via videoconference with a remote physician who was licensed in their state to conduct with the nurse a head-to-toe physical examination and disease-activity assessment.

In order to identify potentially eligible participants, we partnered with the CARA Registry, which I described to you before.

Basically we asked the CARA Registry to provide a list of potentially eligible participants, which they did. We contacted them through emails, physical letters, and then started a phone campaign.

The first thing we learned was that in general, people did not answer our phone calls, but of the people who answered our phone calls, more than

half were interested in the study and actually scheduled consenting calls.

So I mentioned this was a pilot study. Our original goal was to enroll 20 participants. We met that goal in ten days.

So because of the overwhelming enthusiasm for this study, we increased our sample size to as many as we could afford, which was 26, and added an additional 18 participants to a backup list.

This slide shows some selected demographics of those 26 participants, and the map on the right shows, highlighted in red, the states that were represented in this study.

Although our numbers were small, we were pleased to see that self-reported race and ethnicity looked a little bit more like the U.S. population with lupus, as compared to traditional lupus clinical trials.

Although, as discussed before, we did have a lot of people who self-selected race as "other."

In terms of study operations, we found this was highly feasible. So we conducted the entire study from first patient, first visit to last patient, last visit in under ten months, and that includes the six months of follow-up.

We were able to conduct 97 home visits, collect 94 urine and 88 blood samples and nearly 4,000 dosing records on hydroxychloroquine. And note this all occurred in the first year and a half of the COVID-19 pandemic.

On the right-hand side, you can see responses to our satisfaction survey. Overwhelmingly, our participants said they felt comfortable, that they would take part in a study like this again, and actually that they preferred this over a site.

You can also see some of the selected comments, which I think highlight the experience, especially during the COVID pandemic.

So we learned a lot from this study. I think overall we found that this direct-to-family design was desirable, feasible, and satisfactory in

the pediatric lupus population.

And although this was a small pilot study and a niche population, we think this is a potentially promising approach to increased geographic and other types of diversity in pediatric clinical trials. That's not to say there weren't challenges and limitations; of course, there were.

First thing to consider, in terms of safety, so by design, we selected a medication with an incredibly safe profile that's already prescribed and managed per standard of care. And our intervention was actually this medication management device that was incredibly low risk.

That's not to say other types of invention -- or interventions -- excuse me, can't be studied with this type of design, but will require some additional considerations.

We did find that as it turns out, location matters for having study team members that were licensed and able to travel to families' homes.

Technology and data integration, this

actually ended up being a huge thing; could be a separate talk on its own. From a scientific standpoint, we did have a lot of additional considerations in terms of dealing with data quality, device use or misuse or malfunction, what to do with that.

And then we did require a complex data integration flow that we fortunately had the resources to build in-house, but did collect data streams coming from different devices and different platforms.

From an equity standpoint, in terms of technology, we wanted to make sure that we weren't simply trading one barrier, like transportation, for another barrier, like having a smartphone.

So we did provide a study iPhone for all participants to use for the duration of the study. We also downloaded all of the study apps on the phone before we gave it to the family to help with potential issues with digital literacy.

We did, however, require that the families have access to wifi or cellular data. So

that's an important limitation and something that definitely needs to be considered from the beginning for these types of studies.

We also found that -- I think has already been talked a little bit about today, but I think there will be more to come about the critical importance of partnerships.

So we had a wonderful patient and family advisory group that we involved from the very beginning to help design the trial, determine what would be reasonable to ask families to do in their homes.

We involved the CARA Registry, as I mentioned. We also had great partnership from the Lupus Foundation of America, just to name some of our partners here.

If you're interested in learning more, we have a couple publications and hopefully our primary adherence analysis coming soon.

So with that, I would like to acknowledge our fearless leader and principal

investigator, Stephen Balevic, who will be on virtually for the upcoming panel presentation.

I'd also like to acknowledge and thank everyone else mentioned on this slide. I wish I had more time to thank you all individually.

I'm happy to address any questions later or by email, and that's all I've got for you. Thank you.

MS. MULUGETA: Thank you so much Rachel. Our next talk is actually a duo. We have Ted Love, who's the chair of Board of Directors at Biotechnology Innovation Organization, or Bio, as well as Bella Oguno, who's vice president of Development Operations at Nuvig Therapeutics. I'll turn it over to Bella.

MS. OGUNO: Do we have Ted on the line?

MR. LOVE: Yes, can you all hear me?

MS. OGUNO: We can, Ted.

MR. LOVE: Okay. Great. Well, I'll get us kicked off, and then I'll turn things over to Bella.

The first thing I want to do is thank everyone for putting together this conference. I've had the benefit of listening for much of the morning. It's been absolutely excellent.

I'd also then like to begin with a few words about sickle cell disease and about Global Blood Therapeutics, because much of what we're going to talk about is very relevant to specific challenges that we face in pediatric drug development.

So starting with sickle cell disease, this is a relatively rare disease in the U.S. It affects about a hundred thousand people in the U.S., so it is a rare disease.

It actually results from a single amino acid change on hemoglobin, which unfortunately results in profound anemia in affected individuals starting at about 6 to 9 months of age.

Many people classically know these patients suffer from severe pain crises, but what's less appreciated, quite frankly, is that they all suffer from chronic organ hypoxemia.

And as a result, they die typically in their 30s and 40s from chronic organ failure. And that's really what GBT was focused on solving.

The sickle cell population in the U.S. is more than 90 percent African Americans, and quite frankly, solutions for sickle cell disease have been chronically under-invested in by our government, as well as by industry, and the patient community was very aware of it.

The fact that our patients were predominantly black and brown and often poor meant that we were focused on a patient population, which was not only historically poorly represented in clinical trials, but who had often had very poor experience with the medical system, with the significant amount of distrust for the system.

So GBT was really focused on solving the disease, but also solving a lot of the social issues around the disease.

The first note that GBT worked on is now approved. It's called Oxbryta, and the

development program, which you'll hear more about from Bella, focused on helping individuals all the way from 6 months old all the way to more than 60; patients occasionally live that long.

We started the development plan actually in a patient population that was greater than 12, because we wanted to focus on patient report symptoms, which obviously at a certain age you could not collect. And we also initially only had a tablet formulation, which was not suitable for many children, less than 12.

This was actually the HOPE study, which was the basis of the approval. This is a fairly large study of 274 patients if you want to read about it. It was published in the New England Journal of Medicine in June of 2019.

And just in terms of the pediatric component, 16 to 18 percent of the participants in the study were, in fact, under the age of 18.

And the FDA did use extrapolation, which was something mentioned earlier, to support the

approval in that less than 18- and greater than 12-year-old population group.

We also agreed with the FDA to conduct a confirmatory study to show stroke risk reduction, as measured by TCD, in kids in the age range of 2 to less than 15. This was called the HOPE Kid's Study and again, it was a sizeable study of 224 kids.

Our plan was then to lower the indicated age to 4 to 12, and then ultimately to down to 6 months by using extrapolation, again, with the FDA supporting safety, as well as continued efficacy as measured by reduction in the magnitude of the anemia these patients suffer from, and these work for smaller studies.

The last thing I want say is that sickle cell disease is rare in the U.S., but it's highly prevalent in a number of countries, particularly in the sub-Saharan African countries.

Therefore, GBT actually had the opportunity and, quite frankly, as you'll hear about from Bella, the challenge of not only enrolling our

studies in the U.S. and Europe, but also in many countries where clinical trials have rarely been conducted.

Another challenge is that the treatment and death rates for sickle cell disease can vary dramatically, particularly in geographies in sub-Sahara Africa. And that's something that we had to, of course, navigate in collaboration with the Food and Drug Administration.

So with those high-level -- I'll turn it over to Bella. And I really want to give a huge shout out to Bella. She led the team that really did all the work to do these incredibly difficult, complex studies all around the world.

So I'll turn it over to you, Bella.

MS. OGUNO: Thank you, Ted.

All right. So with that lovely introduction, I'd just like to point out the work that we did at GBT to support the enrollment of our sickle cell studies.

So we were really energized around

serving a sickle cell community, and this is an understatement.

From Ted on down, we partnered from the very beginning with CBOs in the U.S. and the E.U., tried to understand the landscape by identifying the key opinion leaders and then also the physicians that were treating the patients. Where are they? What can we do to help, and how do we support the implementation of clinical trials?

So in the U.S. -- you see in this slide here, we're looking at where are the sites, but sometimes when you're looking at the sites, that does not overlay where the patients are, and there's a disconnect, because those communities or those hospitals might not be conducting the clinical trial, so you don't have access to that patient population.

And that was one of the challenges that we had. We know where they are, but do we have clinical trials or clinical research staff to support executing that clinical study?

And as Ted mentioned, the prevalence in

the U.S. is not as high as it is in the ex-U.S., specifically sub-Saharan Africa. So we saw this as an opportunity to augment our recruitment and pivoted towards the sub-Saharan Africa.

And that came with a lot of questions and some challenges that we really try to address. I call this "Looking at a diversity within the diversity"; right? We know the patient population, but what else can we do?

And I also call this the "Era of yes, and." So once we made the commitment to go to sub-Saharan Africa -- and we went to Egypt as well and Middle Eastern countries, the challenges and the considerations came up.

So the logistical challenges, well, how are you going to get drug in? How are you going to get lab samples out? Yes, and let's work with vendors that can support that.

So collecting samples within Africa and testing them within Africa and having method validation transfer, so that could be done.

All right. How do you address the expertise challenges? Yes, and let's train the physicians. Let's have training seminars. Let's go there to understand their perspective.

And let's not forget they see a higher number of these patients in the world. They know these patients; they know this disease.

All right. What about the resource challenges? Yes, and let's help them build capacity. Let's help them identify the resources, study coordinators, nurses, training, so they can conduct a study.

Okay. What about the logistical challenges from conducting the trial perspective? Yes, and let's provide that to them. Let's understand -- for example, someone mentioned wifi and access to the internet, that can be challenging sometime.

How do we support that in sub-Saharan Africa where that's a challenge. Or even electricity where you're storing samples, and they need to be

refrigerated before you ship them out. Yes, and let's give them that -- right, and have generators and backup generators, so they can conduct the studies.

So we were constantly faced with the challenges and the response was, "Yes, and how do we support this community to be able to implement these studies?"

And how do we do this? I think one of the aspects that was really important to us -- if I can advance this slide, is the "how." One of the critical aspects is engaging the sub-Saharan African team early on, not just in time.

So in 2019 is when I started going to Africa to understand who are the key opinion leaders here, who are the physicians, who are the community based leaders that we need to be aware of, and also the cultural aspect is really important.

It's not just understanding who they are, but how do we communicate. And it's not just picking up the phone and saying, "Do you want to do this clinical study?" It's being in person.

So I went there several times to understand that hierarchy and how to get them engaged, so other team members can also participate in that clinical study.

So it took time to build that trust. It took time to build the trust also of the parents who were conducting -- who would be consenting for their children to participate in the clinical study.

And I'll give an example of how that was really important for us to build that trust at that level. There was a listening tour before we started implementing the study.

There was still a lot and there still is a lot of stigma around sickle cell. So with that comes the treatment, the medication that they don't even want to access, because it gives away that they have sickle cell; right?

Transportation is a big thing in Africa. Some of these patients are coming from two to three hours away. So imagine having a 2- to 3- to 4-year-old taking a bus, not even coming by car, but

taking a bus to come to the site, being there all day, and then having to go back.

So making sure that we were aware of those challenges and the way we developed the protocol, the way we make sure that they had the transportation was also really important for us as we understood how do we implement this study in sub-Saharan Africa.

Equipment as well. And one of the things when we were engaging with the KOLs and the team members -- I will never forget this discussion, I had a doctor in Kenya say, "Well, you want to access our patients and get our data, take it all out, and now, do we have access to that data? And are we even going to have access to that treatment later on?"

So these are the difficult discussions that I brought back to Ted -- I brought back to GBT, so we can be intentional around developing a response, not just a knee-jerk reaction to placate those concerns, but to really address how are we really going to collaborate with this patient population --

with this region to build trust, so they feel confident in enrolling their children in this clinical trial.

So that trust exercise took over a year. We started in 2019 before we implemented the study, and then in 2020 everyone knows what happened.

So in 2020 everything came to a standstill, but we still needed to move forward. And I remember specifically in October of 2020, I said, "Ted, I have to go to Africa. No one is traveling. No one is doing anything, but I have to go to Africa. I have to go to Nigeria to do the training for TCD."

This is transcranial Doppler training to conduct a study. So we needed to train the sonographers, each of the sites in Africa, and we needed participants to do that, and that's children from 2 to 10 or 12 years old.

So imagine having to coordinate that at the height of the pandemic in 2020. Coordinate a hotel that will let you do it. Coordinate informed consent of patients and the children, coordinate COVID

tests for all of them, coordinate transportation, coordinate the space, make sure there's enough social distancing, coordinate technology, so we have people from the U.K., from the U.S., all over the world dialing in to ensure that the training is being conducted appropriately.

I think this is the level of collaboration and commitment that it took from not just GBT, but our partners, whether it's vendors, the parents, the regulators, the physicians, to ensure that we completed the training on time.

And I'm happy to say that no kids were sick; everyone was able to complete the training. You just have to make sure there's a lot of food, a lot of coloring books, cartoons; everyone can run around and get tired and then do the training.

But it took a big effort and trust, and that was also an opportunity for the parents and caregivers, for me to share the importance of a clinical trial.

Some of these parents had never heard

of clinical trials in the first place or much less participated, now have their children participate, or have heard of GBT or even questioning a sickle cell study. Yeah, we have the greatest prevalence but we've never even heard of the actual opportunity to participate in a study.

So that was one of the benefits that we garnered from collaborating and collaborating early on and taking some risks, quite frankly. And this just elaborates again, what we implemented and how we were able to be successful in executing this study.

It was continuous process improvement, risk mitigation, execution, and revisiting that strategy day in and day out. There were always challenges that crept up. That's just the nature of clinical research 101 and being in the region.

But how do we continue to show that collaboration and be determinant in how we execute and recruit in the study?

And again, with the support of the FDA, as Ted mentioned, after implementing the study in the

sub-Saharan African region, we were able to recruit the study fully and quickly with those countries.

And I think the key lesson here is not to be deterred by how difficult it is, because everything that's difficult is not what we're doing. But also having a vision for how you're going to get it done and having that commitment internally and externally dedicating the resources.

This took a long time and it was a heavy lift again from our organization from having the right team members and the resources financially to get this done, because we're also helping to build capacity.

I mentioned the TCD machines. We developed a process that after we were able to do the training and they use this for the study, they could keep the TCD machines to continue that assessment for their patients long term; right?

So how do we continue with capacity building when we're working with these countries, when we know that the resources are lower, but the data is

just as valuable, and working with those patients are just as valuable?

The last slide is not here, which is why do we do that? And I remember Ted always said, "Because we need to do the right thing for patients and that means all patients, and when you do the right thing for patients, we do the right thing for our organization as a company, but also the development of a molecule or the drug."

And that's all I have. Thanks, everyone.

MS. MULUGETA: Thank you so much, Bella and Ted. Now, I'm going to ask Lauren Wood-Heickman, who is a clinical reviewer at the FDA, to provide the last talk before we move into the panel discussion.

MS. WOOD-HEICKMAN: Just testing it out. Good afternoon.

Can I move the presenter view down? Can you move it to the left, please? Thank you.

Okay. Great. So my name is Lauren Wood-Heickman. I am a pediatric endocrinologist and

medical officer in the Division of Diabetes, Lipid Disorders, and Obesity.

And the purpose of my talk today is to discuss diversity in pediatric type-2 diabetes trials, illustrated by an example of an assessment I performed on a sample of trials submitted to the FDA in the support of approved drugs to see how they measure up in terms of representing our diverse population of patients with pediatric type-2 diabetes.

Also, I'll be referring to type-2 diabetes as "T2D" throughout this presentation.

Oh, sorry. There we go.

So please, note the views expressed in this presentation are mine and should not necessarily be interpreted as those of the FDA. I have no financial conflicts of interest to report.

First, I'm going to provide an introduction to youth onset type-2 diabetes, or T2D. Then I'll discuss FDA's approach to encouraging representative studies through regulations impacting pediatric trials and the new guidance related to

diversity action plans and how it applies to pediatrics.

Next, I'll highlight some unique challenges in conducting clinical trials in youth-onset T2D. Then I'll discuss an assessment of representativeness for a sample of pediatric trials submitted to my division.

Lastly, I'll discuss lessons learned and future directions on how to move forward with this information. Type-2 diabetes, or T2D, in youth is a serious disease with an aggressive clinical course.

Complications of diabetes develop rapidly in children resulting at a high risk of debilitating complications like cardiovascular disease, kidney, and eye disease by young adulthood.

Mortality in children with T2D is two to three times higher than the general population. Diabetes is common, affecting 1 in 10 Americans, and approximately 90 to 95 percent of cases of diabetes are type-2 diabetes, according to the CDC.

However, youth onset T2D is relatively

rare, so versus 1 in 10, it's one in 1,500 U.S. youth under 20 who is impacted by type-2 diabetes. And the prevalence of approximately 43 million U.S. youth from ages 10 to 19 in the U.S., approximately 28,800 have T2D.

And as for incidents, each year about 5,000 youth under 20 are diagnosed with T2D. Although, this is increasing. And in contrast, greater than three times as many youth in the age group are diagnosed with type-1 diabetes.

And unlike type-2 diabetes in adults, which tends to be equal among females and males, type-2 diabetes in youth differentially impacts females versus male youth.

While youth-onset T2D is still relatively rare, there's a rising number of diagnoses in children every year. The yearly rate or annual incidents of newly-diagnosed youth with T2D almost doubled from the years 2002 to 2018.

And in the U.S., racial and ethnic minority youth carries the largest burden of this

increase in youth-onset T2D.

As shown in the figure below, looking at the annual incidents of newly diagnosed T2D in youth ages 10 to 19 years over time -- so with years 2002 on the left and 2016 on the right, along the bottom of the chart, an increasing number of diagnoses can be seen among American Indian youth in red at the top, non-Hispanic black in purple, Hispanic in blue, and Asian and Pacific Islander in gray, compared to their non-Hispanic white peers, the line in green, with the red dotted line showing the average incidents for all youth over time.

So as you can see, because there's a differential impact on youth and there's an increasing number of diagnoses, this becomes very crucial in order to understand the benefits of the treatment in all populations.

So evaluating the safety and effectiveness in medical care and treatments for a representative and diverse population is critical to advancing health equity.

For pediatric T2D, there's a disproportionate impact on ethnic and minority youth, including a higher race rate of diagnoses and moreover differences in both health outcomes and differences in risk factors for health outcomes observed by race and ethnicity.

Therefore, representation in youth-onset T2D trials is important in ensuring that positive health outcomes from treatments being investigated apply to all patients.

Now that I've gone through a primer on T2D in youth and the importance of representation in clinical trials, I'll provide an overview of FDA's regulations impacting pediatric trial diversity and the mechanisms by which FDA has used to encourage more representative trials in kids.

On the left, the Pediatric Research Equity Act or PREA, a law passed in 2003, requires pediatric studies for certain drugs and biological products being developed for adults, if FDA determines that the product is likely to be used in pediatric

patients or if it would provide a meaningful benefit over available therapies.

The other mechanism, on the right, the Best Pharmaceuticals for Children Act, or BPCA, passed in 2002, is a voluntary mechanism. FDA requests a sponsor conduct pediatric trials by issuing a written request.

The emphasis here is that the BPCA on the right is voluntary. In terms of the written requests are fulfilled, sponsors may receive an additional months' of marketing exclusivity.

Within the guidance on the right, there's a mechanism for which the FDA has used to encourage diversity, in terms of the BPCA.

So they can encourage that they shall take into account adequate representation of children of ethnic and racial minorities.

So in summary, on the left, there's two mechanisms in which the FDA requires pediatric studies. If they are going by the required mechanism, the Pediatric Research of Equity Act, on the left,

there's less criteria, less requirements.

But if you're going on the BPCA, on the right, there are more requirements, including the requirement to take into account adequate representation of children and ethnic racial minorities.

So for the diabetes division, a lot or most of our studies are conducted under BPCA and have accounted this.

There's also new guidance, the draft guidance for Industry, "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials."

Would you mind scrolling down a little bit in the script? I just want to make sure I get my wording right. Thanks, guys.

Okay. That's okay. Let me pull it down. Sorry, guys. I think I have it written out too.

Sorry, guys. The regulations are really important.

So the recent regulatory draft guidance -- let me pull it up here, was published in June 2024, and it's entitled "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials."

And this draft guidance, which applies to Phase 3 trials or pivotal clinical trials submitted to the FDA, recommends that sponsors submit a diversity action plan that specifies goals for clinical study enrollment by race, ethnicity, sex, and age group.

And so once this guidance is final, regardless of whether sponsors will be conducting pediatric studies under PREA on the left or under BPCA on the right, they will need to come up with a plan for representativeness that takes into account adequate representation of children from racial and ethnic minority backgrounds.

Okay. So now I'd like to set the stage to discuss some of the unique challenges associated

with drug development, in type-2 diabetes in particular, by showing the history and current landscape of FDA-approved treatments.

So in 2000, the FDA approved metformin to be used in youth with T2D. Prior to 2000, insulin was the only FDA-approved medication to be used for this condition until 2019 when Victoza or liraglutide was approved.

Therapeutic options other than insulin or metformin were not available to youth, despite many drugs becoming available for adults with type-2 diabetes.

As shown here, over the last four years there have been a burst of approvals for new drugs for treatment of youth with T2D.

It's important to note that the studies leading to these approvals were prompted by the regulations that I discussed earlier and requiring pediatric trials to be conducted for drugs that would benefit populations.

So this slide highlights some good news

and some bad news. There was a gap in care for youth with T2D prior to PREA or BPCA, which has arguably led to many approvals in this area.

But there was a sizable delay between when drugs became available in adults and when they became available in kids, as highlighted by Pam earlier.

When looking only at the approved drugs pictured in the red box, the lag time on average was 8.6 years between adult approval and pediatric approval with a range from 7 to 10 years, depending on the drug.

So PREA/BPCA are arguably leading to increasing approval in kids. But why the delay? Over the next slide I'll discuss the challenges faced by clinical trials in youth with T2D.

So there are several challenges faced when conducting trials in youth-onset T2D, and despite pediatric type-2 diabetes trials actually being pretty short -- they're typically only 6 to 12 months duration, the time required to complete these trials

have been long due to very slow enrollment.

From a recent published analysis of U.S. Phase 3 or 4 pediatric trials conducted from 2000 to 2020, only 5 of 17 studies, or 30 percent, of the studies met projected enrollment targets in less than 4 years, meaning that the majority of the studies -- so 70 percent, took longer than 4 years to enroll the required number of subjects into the study.

Challenges to enrollment are multifactorial, including restrictive eligibility criteria, a small pool of eligible participants, and lack of dedicated pediatric research infrastructure, among other reasons.

However, as you could likely see, the longer times to enroll subjects in clinical trials contributes to longer timelines to approval of drugs to pediatric type-2 diabetes.

Okay. So now that I've reviewed the unique challenges in clinical studies for youth with T2D, I'm going to present my assessment of how these trials measure up in terms of representativeness.

So my goal was to compare the race and ethnicity breakdown of trials submitted to the diabetes division to the known race and ethnicity breakdown of children with type-2 diabetes in the U.S. This would give me a good sense for how representative the trials are of the diverse population of patients with T2D.

I limited my investigation to five clinical trials conducted for approved drugs. In order to get a feel for representativeness, I needed a good benchmark study to see how studies were doing, and I determined the best source of representativeness data we have for U.S. youth would be the SEARCH for Diabetes in Youth study mentioned earlier by Ann.

So the SEARCH study is the largest surveillance effort of youth-onset type-2 diabetes conducted to date and is CDC-funded, and NIH-supported, and it surveyed physician-diagnosed diabetes in five U.S. states, as well as several American Indian reservations from 2000 to 2020.

And the SEARCH study was designed to

actually represent or overrepresent certain youth thought to be at highest risk for youth-onset type-2 diabetes.

And then CDC actually reports the prevalence and incidence data from the search study for youth-onset type-2 diabetes.

Now, I'm going to present the results of the representativeness assessment, and on the left, you can see the results of the most recent analysis from 2017 for 1,230 patients with youth-onset T2D in the SEARCH study.

As I mentioned before, there's some limitations to this SEARCH study, including overrepresentation of certain groups, and how the SEARCH study grouped the data is a little bit different than how clinical trials report data on race and ethnicity.

For example, the non-Hispanic Asian population in light blue also includes Native Hawaiian or other Pacific Islander, a group that's typically reported separately, so this may not be directly

comparable to how clinical trials typically report race.

So on the right, in an effort to the match the data we get from pediatric clinical trials to what we see in patients with youth-onset T2D, I'm showing the race and ethnicity breakdown for five trials FDA approved for the treatment of pediatric T2D. And it's for 811 subjects.

It's important to note that these 5 trials are global trials, which, in total, 42 percent of the subjects came from the U.S., so 58 percent from non-U.S.

And U.S. subject enrollment in these studies range from making up, at the low, end 15 percent of the study population and to 68 percent at the highest end.

You can see that non-Hispanic black in red, American Indian and Alaska Native in purple appear to be greatly underrepresented, while non-Hispanic white in green, Hispanic in dark blue, and Asian in light blue are overrepresented in the five

global pediatric T2D trials submitted to the agency.

Now, I'm going to show you the same analyses for the 5 studies, but limited to the 339 subjects enrolled only in the U.S.

On the right, I've enlarged the figure a bit to show the race and ethnicity breakdown for the studies a little bit more clearly.

So it looks like the trials are doing reasonably well in terms of representing non-Hispanic black youth in red, with overrepresentation of Hispanic youth in dark blue and non-Hispanic white youth in green.

In the subjects enrolled in the U.S., there's also an underrepresentation of non-Hispanic American Indian or Alaska Native in purple, Asian in light blue, and Native Hawaiian or other Pacific Islander in orange.

But keeping in mind that the SEARCH study on the left isn't directly comparable, as the light-blue Asian category on the left represents Asian, along with Native Hawaiian or other Pacific

Islander youth.

So depending on how you look at this, you could determine that pediatric T2D trials are generally doing pretty well in representation for some groups. But there are definitely gaps where representativeness could improve. This type of analysis allows us to understand areas of focus for future studies.

So in conclusion, this case study identified several gaps in the representativeness of pediatric T2D trials submitted to my division of the FDA, but was also generally encouraging.

So American Indian and Alaska Native, Asian, and Native Hawaiian or other Pacific Islander patients with youth-onset T2D from the U.S. are underrepresented, based on this analysis.

In terms of lessons learned, this strategy could be applied to other pediatric trials' programs to evaluate the relative representativeness of the clinical trials being conducted in order to get to those gaps and ensure better representation in

clinical trials going forward.

There are several opportunities moving forward to continue to address barriers in representativeness, in addition to addressing other challenges in conducting efficient youth-onset T2D trials.

Firstly, in conjunction with the Division of Pediatrics and Maternal Health, or DPMH, we're planning to hold a workshop for pediatric type-2 diabetes in spring of 2025 to further address challenges faced in the conduct of trials in this disease area.

Next, in addition to written requests, our division, and others at the FDA, managing pediatric applications can integrate the 2024 Race and Ethnicity Diversity Plan guidance and to face three pediatric trials designed to address PREA requirements, encouraging sponsors to establish goals early in the pediatric development program for representativeness.

And as for further investigations into

representativeness, I'm also planning to work with a fellow in FDA's Indigenous Knowledge Fellowship Program to further investigate the notable gap in representation of American Indian, Alaska Native populations observed ,since T2D disproportionately impacts this population in youth.

There's more work to be done to further understand what can be done to address gaps in this area.

Thank you so much for your attention. I've learned so much from you and this conversation that we've had together. Thank you.

MS. MULUGETA: Thank you so much, Lauren.

I'm going to ask my co-moderator, Sue Rahman, to join me along with panelists.

So we actually have had close to 500 online participants, and we have a large number of questions we're triaging.

So after the new panelists get a chance to introduce themselves, perhaps we can start with

those questions, while you consider whether you have additional questions for our speakers and panelists.

MS. RAHMAN: Perhaps we can go ahead and get started with introductions by Anvita.

MS. AMBARDEKAR: Hi. My name is Anvita, and I'm a pediatric patient representing iCAN, the International Children's Advisory Network.

I personally am a pediatric patient, and I have IBD, and I am very passionate about advocating for patients and hope to continue that here.

MS. RAHMAN: Yes, please.

MS. DONOGHUE: Hi, everyone. Good afternoon. My name is Martha Donoghue. I'm a pediatric oncologist, and I am the associate director for Pediatric Oncology in Rare Cancers in the Oncology Center of Excellence at the FDA. And I just want to thank everyone for the conversation and for inviting me here today.

MS. ROBINSON: Good afternoon. My name is LaShell Robinson, and I'm the senior director and

head of DE & I in Clinical Research at Takeda Pharmaceuticals, where I lead the company strategy related to DE&I in Clinical Research to make sure that we have proper representativeness in our clinical research trials.

MS. MILLIGAN: Hello, everyone. I'm also with Industry, colleague Lashelle. I'm Ki. I'm a pediatrician. I work at Novartis, and prior to my current role, I've lived and worked in Asia, Europe, and the Middle East in public and private sector jobs.

And I only say this because understanding that housing, transportation, insurance, language, visa immigration status, navigating that as a moving target, I can only begin to understand that before attempting to understand clinical trials at the same time.

Thank you.

MS. EDWARDS: Good afternoon everyone. My name is Christina Edwards. I work at the National Minority Quality Forum in our Center for Clinical and Social Research as the director of Clinical Trials.

National Minority Quality Forum, NMQF for short, is a health research equity and educational and advocacy organization.

MS. RAHMAN: And we're also joined online by Stephen. Do you want to go ahead and introduce yourself?

MR. BALEVIC: Yes, thanks very much. I'm Stephen Balevic. I'm a pediatric and adult rheumatologist at Duke University and a researcher at the Duke Clinical Research Institute.

So I'm wearing my academia hat today and happy to talk about the diversity in clinical trials. Thank you for having me.

MS. MULUGETA: Wonderful. So the first couple questions are actually directed to Rachel and Stephen. So the first question is, was the direct-to-family global trial, could you also comment on the overall monitoring and GCP compliance for such a trial?

MR. BALEVIC: Yes. Thank you very much for that question. Yes, this trial was only conducted

in the United States, and largely because we were still working out a lot of the legal and regulatory implications, you know, that I think are hinted at in your question.

And what we learned when we were putting this trial together -- just to, you know, ensure that we were, you know, meeting clients and also staying within the state medical legal guidelines, we actually surveyed 15 different states, in terms of what their telemedicine and telehealth laws were, because it wasn't totally clear to us that there's a line drawn in the sand between what we would call tele-research versus telemedicine.

And so that gets very complicated very quickly. And so for the sake of time, I won't go into details too much, but you know, it was very important for us to try to navigate a lot of this gray area between what is the practice of medicine versus research across many states and what can be done virtually versus what requires an in person visit.

And so I'm happy to answer more

specific questions and tell you a little bit of the learning that we've have from a medical legal perspective.

But it is a major challenge with virtual trials, and I think one of the things we can do moving forward is try to get some clarity, especially from state medical boards, where there's some uncertainty.

Dr. Mulugeta, I don't know if you had any follow up.

MS. MULUGETA: Just one additional comment. Who provided the in-home nursing visits? Was it one company, multiple companies? Were experienced pediatric nurses a requirement?

MR. BALEVIC: Yes, thank you. That's a great question. So we did partner with a single company that was able -- that they had a network of both in-state physicians and in-state nurses throughout the country.

And so we partnered with them, and they were able to provide home-health nurses through all of

the states we were recruiting.

You know, for a decentralized trial, you don't necessarily need a registered nurse, if all you're doing is, let's say, a blood draw, for example.

But in our case, we were not only drawing blood, but we were facilitating a telemedicine -- and so that required somebody with a medical background -- with medical expertise, you know, to be able to, you know, auscultate the lungs, examine the joints, along with the physician. So that's why in our case, we did use registered nurses in those cases.

MS. MULUGETA: Thank you so much. Any questions from the in-person audience?

MS. COVINGTON: Good afternoon. Thank you very much. I'm enjoying the conference. It's for anyone, but particularly Dr. Heickman.

You mentioned showed some, "gray statistics" about what you compared in the clinical trials versus what you compared, I think, in the real world or what you actually -- the comparison from what

we had before to the representativeness of child clinical trials.

Here's my question. My question is -- it seems like you did a very good job. By the way. My name is Melva Covington, I represent Abundant Life Bible Church, as well as AGAPE Strategic Solutions.

Here's my question. Is it sufficient for us, especially from an FDA perspective, to be able to just say that we're able to collect data from patients that are at the right proportion?

And I say this, because we just conducted a study with PEP!IN, People Empowering People for Inclusion Now, in which we surveyed people -- diverse communities, and 20 percent of them were in clinical trials.

When we asked them about the value of the clinical trials that they participated in, it decreased. So everyone a hundred percent said, "I got into trial; I understood what it was about; I got the -- even protocols."

But when you ask them about the value

that they had once they were through the study, then they were, like -- 55 percent said, "I got no value out of it."

So is just representation enough? Should we be looking at what then is the experience and using the experience that people have to not only develop the protocols and study designs, but to create the experience that people can use and understand and value as they go through these processes?

What do you think?

MS. RANDELL: I think that's an excellent question. I think that you -- so my understanding, I believe that there is inherent value in representation in clinical trials beyond just proportionate representation.

And even though it's a goal to meet, in terms of the disease, this is what the disease looks like. These are the people impacted by the disease.

We need to make sure that the studies represent the people who are going to be treated so that they feel confident that the drugs are safe and

effective in them.

I think that there's questions beyond "Can we get achieve that by meeting those proportions." I think one of the earlier questions was, "What is good?" And I think that's really important to continue to communicate through these workshops. And I'd love to hear from the other panelists too.

The other thing is, with these diversity action plans, they're in the phase of pre-implementation. So it's at this stage where public commentary and public feedback is crucial.

And so there's several guidance documents that tell sponsors what our goals are, but there's also an opportunity here to figure out the best way to implement these strategies and to communicate those things.

So really, I think that's a really great question, and I would love to hear the rest of the panelists thoughts on it too.

MR. LOVE: I'll get that. I think it

was a great question as well, and honestly, it kind of reminds me of the history of colleges in the United States enrolling students of color and sometimes adding women to the student body without making any adaptions.

They just expected those individuals to come in and flourish in the environment, just as the prior students had. And I think it's critical.

In fact, what we're trying to do in these clinicals from home is get information on this patient population, but as someone said already, we're also trying to bring this population into the world of drug discovery and drug development, as well as into the ecosystem of excellent healthcare and participation in utilization of these discoveries when we develop.

So if you're going to do all of that, you really do need to make sure that you're creating an environment where these patients feel just as valued, just as respected, and they benefit just as much as other patients from this setting. So I think

it's a great point.

MS. MULUGETA: Martha, did you want to add to that?

MS. DONOGHUE: Yeah. No. I was pondering the question, because it has so many layers to it, and I would absolutely love to devote a whole workshop to questions like this.

Because I think, you know, what you're asking goes beyond -- you know, it is simply are we thinking about just looking at the numbers and really high-level numbers, and can we pat ourselves on the back if we look at the numbers and feel reassured by them?

And I think, you know, at a bare minimum, it is helpful to know, you know, as the highest-level target or maybe the lowest bar, whether we're actually enrolling patients, you know, with respect to diversity in a way that's equitable.

But just looking at the numbers alone and even those initial numbers is just a start, because I think about our experience in pediatric

oncology where our data is relatively reassuring with respect to representativeness when you look at race.

We also find that, in terms of reporting over the past 20 years in some of the studies we see, that we have huge holes in our data with respect to ethnicity.

We're also not thinking about geographic distribution of patients where, you know, by and large they tend to be, you know, hugging the coast of the U.S., as opposed to more rural areas, thinking about socioeconomics and other factors.

So I think the point you're bringing up by this provocative question, which is pretty easy to answer, because I think most of us would say no -- we can't say that's enough, you know, is it really important?

And I think it's incumbent upon us not only to, like, finish a trial, get the results, and, you know, kind of say, "Okay; let's move on to the next trial," I think it's also really important to do what you're implying, which is -- and what you have

done, is to ask patients and families, "Was this a valuable experience."

Going beyond whether the drug works, which of course we all want them to work, thinking about was this a positive experience; do you think it was worth worthwhile, and feeding that knowledge into future trial designs.

And, you know, I think it's integral to drug development for now and in the future that we are trying to take advantage of that input and incorporating that in the very early stages of future trials.

So thanks for the question.

MS. ROBINSON: And I would just add too, did it improve your experience or opinion of the healthcare ecosystem? Because when we look at one of the main challenges when we're talking about underrepresented populations is the lived treatment that we are getting in the interaction with healthcare providers; right? And that mistrust that exists.

So I would also move a step forward,

did it improve your overall experience and outcome and your opinion of the healthcare system that we're dependent on to improve our health disparities?

MS. RAHMAN: Any other comments from the panel?

MS. UMARETIYA: I would thank you Melva for the question. I would also like to echo what the panelist said and add another question on top of that is, who defines benefit?

So I think now that we have, you know, this beautiful concept of equity of voice, it's actionable through FDA policies.

You know, when we talk about risk benefit or burden benefit, maybe the definition also requires broader stakeholders to bring that into definition and perception of benefit.

MS. RAHMAN: Our next question was from the center of the room.

MS. SARI: Hi. Sorry. I'm Nasrin Sari. I am about to be a panelist in a bit. I'm also a patient and community representative.

And my question is mostly directed at Dr. Heickman, and it's sort of based off of -- I just read an article published in 2023, which basically called for the need of inclusion of Middle Eastern and North African peoples in diabetes trials.

Basically citing that globally, that region, the Middle Eastern and North African region, has the highest prevalence of diabetes in the world.

But with the way that our government, I guess, and our systems characterized and categorize people, it's sort of an invisible group.

And even we could see in a lot of the data that you were citing -- I mean it was a great presentation, but it didn't take that into account.

So I guess what I would ask is -- I'm wondering what the perspective on this is in the field or if there is even a perspective; are people aware of this issue and of this lack of representation?

And I guess anybody who has experience can answer, but it was mostly directed at Dr. Heickman.

MS. WOOD-HEICKMAN: Yes. That's an excellent question too. And Dr. Christine Lee cited that there is a new OMB data collection standard.

A lot of the limitations to these analyses that you can do have to do with the patient level of reporting -- of their self-reporting, and that may be different culturally. It may change over time. People may identify in a different way.

And so it sounds like the OMB standards, they're changing to add North African and also Middle Eastern as a category.

And then they're also allowing people to check multiple boxes and enter, within American Indian, the specific, like, region they come from.

And so we have more data, and so our ability to interpret it will become better. But you're right; we're working with data that was collected ten years ago or eight years ago, in the case of some of these studies.

And we basically -- how they decided to report that data in those trials are how we have to

deal with it.

But another portion of your question is, that these are actually global studies; right? Like, these diseases, we regulate them at the FDA and the U.S., and we advocate for our population of the U.S. to be represented within these trials.

But you have to realize that they're also applying for these drugs to be studied worldwide. And so many of these are global efforts.

So that's an excellent question. We advocate for our population, but we also oftentimes have bigger studies, because they're global efforts. And that's a benefit, but you also have to consider, do some of the global populations represent our U.S. patients?

And they may in some cases, but in some cases you have to -- you develop more questions, based on more data, which I think is exciting, but it also unwraps another layer of onion.

So thank you for that great question.

MS. SARI: Thank you.

MS. WOOD-HEICKMAN: Anybody else?

MS. MULUGETA: Actually, if I can add to the question that Nasrin posed, we had one question specific to Bella and Ted's presentation, which builds on this topic.

Will patients enrolled in Africa be considered representative of African American patients in the U.S. to meet the enrollment goals and diversity plans?

So maybe, Bella, you can get us started, and then I'm going to ask others to chime in as well.

How do we determine whether patients from other countries are representative of U.S. populations?

MS. OGUNO: I'm back here, but I'll let Ted start it, and I can add to Ted's thoughts.

MR. LOVE: You know, it's an interesting question. I don't think we actually had that particular discussion with the FDA.

Sickle cell is somewhat unique. I

think the bigger issue with sickle cell actually is the same issue that we encounter in cancer and other diseases, where the standard of care in that geography is very different than the U.S.

And unfortunately, in sickle cell disease, unlike many of our cancers, prior to GBT, there weren't many differences, because we were basically just using hydroxyurea and occasionally transfusion.

Most patients with sickle cell disease really were not on any kind of treatment for their underlying disease.

So the ethnic issue, we didn't discuss. The treatment, kind of, differential, we did discuss with the FDA, and sadly in many ways the difference wasn't as dramatic as you might expect.

MS. OGUNO: I just wanted to comment on the previous question, in terms of being inclusive Middle Eastern and North Africa.

When we looked at GBT'S study for sickle cell, we went where the patients were. And

when we think about sickle cell, we think of the African descent, but we were also knowing that, or saw the data, where Middle Eastern population was also impacted.

So we were intentional about going to Egypt, Lebanon, and Oman. So even there were challenges there as well, but we really went where the data told us where the patients are and making an effort to recruit those participants.

I wanted just to kind of shout out to the question you had and really being intentional about where you're going and where the patients are recruited.

MS. RAHMAN: I think our next question --

MR. LOVE: And maybe the other thing to add scientifically is that sickle cell disease is a genetic disorder, and there are different genotypes. So we did look at the data also by genotype, whether you were SC, SS, you know, S rated zero.

So we looked at the genotypes, which

probably are more important than your geography. But anyway, we looked at everything.

MS. RAHMAN: I think our next question was from over here.

UNIDENTIFIED SPEAKER 4: Good afternoon. I think my question is for Dr. Randell. Rachel; correct?

With your study you ran it, and it was a great benefit to kind of run it during the pandemic, unfortunately.

Would you run it again, now that the world is open, in a more hybrid scenarios for a lot of people? I know during the pandemic, I had nothing, but times to be at my house, and I specifically knew what time I would be out of my house.

I still had to go on site, but I knew what specific 12 hours a day I would be gone. So I had nothing, but time. I picked up a lot of habits and hobbies.

And I have a -- I guess it's like a three-part too. Did you also have scarcity issues

with hydrochloroquine [sic] during the pandemic and people's perceptions of that due to news that was out there concerning that drug?

And yeah, again, would you run this in a hybrid scenario to see if you would get the same participation and also the same lack of attrition?

MS. RANDELL: Thanks for those questions.

And just, Stephen, I'll take this one.

So first off -- well, it sounds like we had a lot of similar thoughts during 2020 to 2022-ish. In terms of the question of if I would do this outside of the COVID-19 pandemic, absolutely.

So actually, this study was planned and designed well before the pandemic hit and while most traditional research at Duke was basically shut down, put on pause March 2020, we were able to launch this study a couple months later and really, like, went without a hitch.

There were two participant family members who had COVID during the study, but we found

that because of the virtual design, we could offer them an option of just a video-visit-only type of study visit or reschedule with a lot more flexibility than if they were traveling to a site.

I thought -- and I hope the data I shared with you today convinces you of this as well, but I thought the direct-to-family design worked really well, and our patients and their families really liked it.

So I have actually two other direct-to-family studies that I'm currently working on, another one in lupus and another one in juvenile idiopathic arthritis.

So I'm really excited about the opportunities for this design. I think I forgot the third part of that question.

UNIDENTIFIED SPEAKER 4: Oh, did you have scarcity issues with --

MS. RANDELL: Oh, with the medication? Oh.

UNIDENTIFIED SPEAKER 4: -- getting

that specific drug?

MS. RANDELL: Yeah.

UNIDENTIFIED SPEAKER 4: And then what were people's perceptions or did you take any feedback on people's perceptions of that drug per what was being dispersed in the news?

MS. RANDELL: Oh yeah, great question. So fortunately, not an issue for this study. Hydroxychloroquine was already being prescribed by the participant's doctor -- their healthcare provider, per standard of care.

This is a medication that is generally prescribed for a very long time for lupus. So the families who were in the study did not encounter the difficulties, I think, that you're referring to.

And the timing occurred just far enough into the pandemic that the, like, mad rush on the world's hydroxychloroquine supplies had kind of, like, abated a little bit, so it wasn't an issue.

But certainly great questions to think about for any type of direct-to-consumer, direct-to-

family design. So we're not providing the study drug, which has some benefits, but it also relinquishes our control over being able to control the study drug and the supply and whatever else may happen.

So in this sort of decentralized design you do -- that's just one example of different aspects of the trial that you're then decentralizing -- putting into other people's hands to manage that are out of your control.

Thank you.

UNIDENTIFIED SPEAKER 4: Thanks.

MS. MULUGETA: So I know we have several questions in the audience, but I want to make sure we give our patient and community representatives a chance to speak as well.

So you both have heard throughout the day perspectives on how to make trials more inclusive, but as a patient, what do you think are things that are key to making trials more inclusive?

Maybe, Anvita, we can start with you and then, Christina, if you can chime in.

MS. AMBARDEKAR: Yeah, definitely. Thank you so much for the question.

So I think the main thing is just making it available to people, making them aware that there are trials. I know for me personally, like I knew what clinical trials were and that they were conducted, but I never knew if there was one for me -- if there was one that would be the right fit for me.

So kind of even just providing a guide on how can you figure out if you know enrolling in a clinical trial is right for you, and then also kind of just making it more aware that there are trials out there that are looking for pediatric patients to enroll.

MS. MULUGETA: Thank you.

Christina.

MS. EDWARDS: I'll talk about this a little bit in my presentation, but I think what I will focus on is engaging with the community and making sure your approach is patient centered.

You know, you always want to get their

perspective. I think they are the bottom line essentially. So just making sure they are -- from protocol, development, planning, that should be your focus is the patient's perspective, and what do they need -- their wants.

MS. MULUGETA: Thank you.

MS. MCKENZIE: I have one comment and then a question for the patients. I'm Jennifer McKenzie. I am a pediatric nephrologist that works at Boehringer Ingelheim. It's a pharmaceutical company.

My first comment is about the diabetes example that you used for the diversity plan. I think that is an excellent example, and it was very cool to be able to see the overlay of what's happening in the trials versus what's happening in the United States.

I work in a space where we do not have that data. I can tell you what's happening in Southern Israel, but I can't necessarily tell you what the prevalence or incidence is in the United States or even globally.

So I think that some of those other

diseases that don't necessarily have that natural history data are going to struggle with coming up with diversity plans that mimic the population.

My second question is for the patients on the panel. Pediatric academic centers are the primary places where we are able to do clinical trials. They're not everywhere; right? This a very finite resource, and that's where most of the clinical trial sites are going to be for investigational drugs or devices.

If you found out that you were eligible or might be eligible for a clinical trial that was distant to your site or not associated with your primary hospital, how willing would you be or do you think your peers might be to travel longer distances or see people that you are unfamiliar with in your treatment?

MS. WOOD-HEICKMAN: So for your first question, that's something that I have observed as well. I think that diabetes has benefited from the fact that -- has rich data.

There's rich data because of the fact that diabetes is so prevalent in adults, pediatric diabetes community has benefited from that.

But then also that the type-1 diabetes community and type-2 diabetes communities came together, in terms of research, and did the SEARCH study. So they joined in order to create this data from a partnership with the CDC and the NIH, who recognized that it was it was an issue that was evolving.

And so for rarer diseases, that's always a challenge, in terms of getting that data. So I can just acknowledge that challenge, but I can't speak to it too much.

And I know the question was for you next.

MS. AMBARDEKAR: Yes. To answer your second question, so personally, for me, I think traveling a little bit far for a clinical trial would really depend on two factors. First one is, what time of day is it? You know, is it during classes? Is it

during a traffic time?

Because a lot of these times these centers are in big cities where traffic is a big factor than just the distance.

And then also, how much is the trial going to benefit me? Is it more to, like, make me feel better, or is it maybe, like, testing out some new imaging or something like that?

UNIDENTIFIED SPEAKER 5: And just to add to that, I think it depends on the disease state; right? When we're speaking about type-2 diabetes and type-1 diabetes, it's a little more prevalent.

But taking that to a rare case, I can speak from experience, where we did have patients that boarded planes, because they were going to the centers where the Centers of Excellence were, knowing that they would actually get better care -- right, because that person was a Center of Excellence or that center was that physician.

So I think there is a little bit of nuance with that when there's a higher disease

prevalence, maybe not as much willingness, but if it's a rare disease, we have seen patients and families really take leaps and bounds to get to clinical research.

And I think we have to create our budgets and our contracts when we're talking about us as pharmaceutical companies to account for those nuances.

Thank you.

MS. RAHMAN: Take the next question from this side of the room.

MS. MCMAHON: Hi. Dr. Ann McMahon from the FDA. This is a question for Doctors Randell and Balevic.

My question is -- and maybe I missed this, it's possible that I miss this, but I wondered whether it was possible that this model of providing care is going to be something that is way too expensive for anyone to ever do, or whether it's possible that routinely this type of thing could actually be done?

MS. RANDELL That's a great question.

Oh, sorry. Go ahead, Stephen.

MR. BALEVIC: Okay. Great. Yeah. Thanks very much for that question.

So I think you hit on a very important point, which is the decentralized trials really hinge very closely on technology, and, you know, technology is really that key -- you have to be able to reach, you know, families in their homes where they are.

That requires, you know, not only telemedicine software, but all these decentralized, you know, protocols and nurses and centralized IRBs.

And so that infrastructure can be expensive. But one of the great things about technology is that it can become less expensive over time.

And so it really -- this is, I think, a model where, with the right investment and academia and industry and regulatory sort of partnerships, that cost can be driven down, and I think it could become a regular model.

I'll pass the mic to Dr. Randell.

MS. MCMAHON: Thank you.

MS. RANDELL: I was just going to say, I wish I could answer that question in, like, three years from now, because the current project that I'm working on is to try to replicate the things that went well in iPERSONAL on an NIH K23 research budget, which is much smaller.

But for example, instead of paying a home-health nurse to travel to family's homes, maybe we can try something like a self-collected blood sample that the participant and their family can do at home and simply ship back to us.

Just as an example of some areas where we could take lessons learned from this type of trial and try to replicate them at cheaper or maybe in something that's like a hybrid between a traditional site-based and a fully virtual trial.

MS. MCMAHON: Thank you.

MS. RAHMAN: How about for center of the room?

MS. HILDEBRAND: Yeah. Heidrun Hildebrand from Bayer, again. Also question or maybe comment to the decentralized trials. I think that's a great example, and as I come from Bayer, you know, we also work with you on some of decentralized activities, but mainly in the Phase 4 or in the observational study.

And I think also what you showed here is a clinical trial, but more in the Phase 4 setting. And I think the challenges might be a little bit higher when we go to pivotal studies, but I also think that decentralized technology is a great thing, and it is not black and white.

Because we, in industry, I think, most of the companies in the room do that in the meanwhile. We use certain elements of decentralization to go specifically into pediatric studies where we do a part of it.

But our learning is also that there are high sharing just with investigators, because they don't want to be our technology hub.

So instead getting the patients, they do the work. And we also have families who tell us they want to get out of some of these decentralized activities, because for them, the burden is even higher than going into the center and have the doctor managed everything or the study nurse managed everything.

So I think it's a fine balance what we have to do. I think it's a great future, but it's a great balance, and especially if I look to the sickle cell example.

Going into regions outside of Europe or U.S. or even in some of the European regions, you may not have the data infrastructure to do that. So I think it's a fine line.

MS. MULUGETA: Thank you so much. Maybe a question to Martha, and there's a second aspect that's industry specific, so maybe LaShell and Ki, if you can take that.

So the question is, does the FDA foresee requiring sponsors to develop formal diversity

action plans as an adjunct to pediatric study plans?

And the second question is, what is the current experience with industry, including diversity plans or plans to include diverse populations within the pediatric study plans?

MS. DONOGHUE: Okay. thank you for the question. So if I'm understanding it correctly, you're asking whether FDA anticipates requiring diversity action plans as part of the pediatric study plans that are part of our requirements under PREA that Dr. Heickman had spoken of earlier?

I can't speak for FDA in that sense. And also, I'm coming from oncology; the scope of most of our pediatric study plans are limited to Phase 1 and 2 development, whereas the diversity action plan guidance really speaks mostly to phase three development.

So would I like to be able to require them? Absolutely, in oncology. But short of having a requirement, I will tell you that when we are reviewing our initial pediatric study plans that are

coming into oncology, we are asking those questions.

We are saying, "Please, describe and tell us how you are anticipating, you know, enrolling a representative population. Please, speak to the sites that you're going to enroll. Is your trial going to be run through a cooperative group? How are you going to assess whether you're achieving representativeness?"

So we are asking those questions and, you know, we're asking for answers and reviewing them as part of, of our review.

Having said that, it's -- and I think it goes to some other questions that others have alluded to. These are generally smaller studies -- 60 patient studies, rare cancers, rare subsets of rare cancers.

And so, you know, I personally don't want to add additional impediment to efficient conduct of those trials, but it's a balance.

And I think part of achieving our mutual goals is really to make sure people are

thinking about this and doing, you know, what's right to try to, to the best of our ability, ensure representativeness to the population that has access to these trials.

Because, you know, parents of pediatric patients and pediatric patients themselves with cancer, you know, they are loud and clear telling us how important it's that they have access.

MS. MULUGETA: Thank you.

MS. MILLIGAN: Yeah, I'll start, and then open to LaShell.

So I think, you know, this kind of -- so the question on, you know, sponsors and diversity and pediatric trials, I think it's multifaceted.

And it comes back to the principle that we approach pediatrics with is, before we go into a vulnerable population, is there a prospect of direct benefit to that population?

And are we doing everything to reduce the investigational risk and investigational burden as much as feasible? I think we heard really good

approaches on that earlier today -- data science, real-world evidence.

And then the other thing is when we have no other option, but to do a randomized or a prospective study, does that study answer the research question?

So are we able to generate the data that conclusively gives us and the regulatory decision makers information on the drug's efficacy, safety; is this the right dose?

So there's a lot of uncertainty. And I think one thing that I want to highlight just historically, in terms of the R&D ecosystem, there was a time not too long ago where data for drug development was mostly men.

So we changed that. Then there was women. And then it was mostly adults, and then we changed that, and then there was children.

So I think my point is we are equipped to do this. I don't think that we have the answers to -- you know, we don't have all the answers, but we

are equipped.

And then the other part of that is there have been some real-life success stories. So also, LaShell and I were talking. So some of this, you know, you'll hear from her also.

During the COVID pandemic, there was a public/private partnership to look at repurposed medicines for COVID. And one of these studies, the ACTIV-6 study, actually met and exceeded its diversity target. This was not in pediatrics, but it did that through real-time monitoring and pivoting for engagement.

And on that one for the public/private partnership side, it elevated all stakeholders' voice, including community and patients so that community and patients also had access to review trial metrics and suggest how to pivot and meet diversity targets.

So that was a very recent win, and it was something that I just wanted to share. And I'll turn it over to LaShell.

MS. ROBINSON: Absolutely. And I think

it's important to celebrate the successes, because as you mentioned, progress has come. I mean, obviously, there's more work to do, but I think it's important to highlight that.

And also with proactive planning, so there was a question about whether diversity action planning can actually work, and with proactivity and starting from the very beginning, that always sets you up for success when you're thinking with the end in mind, and you have at least something to start with.

We had great examples during the COVID-19 pandemic across multiple companies where we actually saw them meet trial metrics, because there was a concerted effort, and there was even real-time pivoting.

And going back to one of the calls on the diversity action plan is around trial management. How are you actually going to monitor the metrics?

And I can't underscore the importance of looking at those metrics in real-time to make real-time decisions. So for example, really vetting your

sites from the very beginning, and not only looking at what they're reporting is their patient population, but does that actually match the ZIP code, and does that match the historic trial data?

Because for a lot of these clinical sites, they've participated in our clinical trials before, and that can tell you a lot about cultural competency training that may need to be in place or even helping them with community engagement if there's a lack of representation in the actual practice.

And then taking it one step further, when the trial is actually enrolling, and looking at those metrics in real-time to see who is enrolling as you expected, and if not, approaching those sites.

A perfect example that we were speaking about was, there was a site that really said that they were doing great with diversity, and that was part of the reason that we actually selected this particular site for participation.

But as we were watching during the trial, and I was asked to approach that particular

site to get past practices, I noticed that it was like 90 percent white participants. Oh, there's a problem.

So in reaching out to that investigator, they were not even aware that was their enrollment. And as we had a further discussion, she mentioned, "Oh, you know, I don't think I ever got the Spanish ICF."

In addition to that, she also mentioned, "I also don't remember us getting those materials that were translated into multiple languages that you mentioned. We don't have those. This is all word of mouth." And so that real-time engagement and actually having an action, it becomes extremely important.

And so, again, proactive planning, but also having a center that's monitoring those metrics in real-time, so you can make those decisions and pivot as needed, can really set you up for success in meeting those metrics and also is the reason why you need a plan.

MS. RAHMAN: Thank you. We have

reached our time, but please join me in thanking our panel very much for an excellent discussion.

MS. MULUGETA: All right. So we're going to take a quick break and reconvene at 2:15, so please come back at 2:15.

(Off the record.)

MS. MULUGETA: We're going to go ahead and get started, so if you can, please find your seats.

We're going to continue with the agenda. The next panel is a community engagement and trust building discussion panel. And I'm going to turn it over to my colleague, Carla Epps, from the Division of Pediatrics and Maternal Health.

MS. EPPS: All right. Thank you. While people are coming up, I'll just quickly introduce myself. Yes. I'm Carla Epps. I'm a pediatrician with the Division of Pediatrics and Maternal Health here at FDA.

Really thrilled to be part of this meeting. Let's see. Do we have everybody that's

going to be in this panel. Come on up, folks. Come on up.

-- have everybody up here. I'm going to get started with the questions. What I'm going to ask is everybody to just introduce yourselves when you speak and hopeful we'll start with the folks who hadn't had a chance to speak yet today.

Let me just start off before we get into the questions. So this panel discussion is on community engagement and trust.

And I was struck by the conversations this morning about things we are doing and that we could do better that included things, like keeping a track of, you know, who is involved in the trials, using things like extrapolation and AI, that speak a lot to headcounts, and that's some really important quantitative information.

But then I heard later on, discussions about what was the value and what it felt like to be in a trial. And I guess I'm going to start off by saying, as a member of a couple minority populations,

with all the multi-ethnicity we have in our country, being a part of a group or community doesn't mean you feel included.

And I'll say that just as a physician. And there's still times when, you know, yes I've got the degrees and everything. That doesn't mean that people make me feel included in that community.

And so I think it's important to talk about how we measure people feeling not a part of a trial, but included in a trial. That's a very different thing.

So on that note -- and it's a hopeful note, I think, let me get started with the questions with folks.

So the first question I want to ask you all around community engagement and trust is, what does the word "community" mean to you?

And who has not had a chance to speak yet? Has everybody had a -- no. So let's start first. Go ahead, introduce.

UNIDENTIFIED SPEAKER 6: And do you

want us to introduce ourselves?

MS. EPPS: Yes, please.

MS. KIPP: Good afternoon. I'm Dr. Billie Kipp. I'm an enrolled member of the Blackfeet Tribe, and I am an indigenous child psychologist.

MS. SARI: Hello. I am Nasrin Sari. I'm here as a patient and community representative. I've had some experience, you know, with various different positions as a patient. Yeah. And I'm here representing various different groups.

MS. DAVE: Hi, everyone. I'm Sneha, and I am a patient and also the executive director at Generation Patient.

MS. WILLIAMS: Hello, everyone. My name is LaToya Williams. I am the community clinical director at Inside Edge Consulting Group, which is a healthcare consultant firm, and we bridge the community with underserved communities and biopharmaceutical companies.

I'm also serving as a pediatric patient from the past with lived experience and how it's

translating into my adult experience.

MS. AMBARDEKAR: Good afternoon. My name's Anvita, and I'm here as a patient representative and on behalf of iCAN, the International Children's Advisory Network.

MS. EPPS: Thank you. So, Dr. Kipp, maybe you could start us off, because I don't think the group has had a chance to hear from you about what the word "community" means to you.

MS. KIPP: Well, I think community is defined by where you come from and what group you're with. And so for me community means tribal community.

And tribal community is a collection of folks who have same beliefs, practices, and value systems. And oftentimes in tribal communities, and that's where I'm going to speak from, is we're very closed systems. So we're on reservations; we're very isolated, very rural.

And just to show you how important a closed system like that is to medical health, when the COVID came and started wiping people out, the tribes

across the nation start closing their borders.

Because you have a collective people who live there and who have been there generations, you know -- there's generations of people at home on my res, and so they start closing their borders in order to help mitigate COVID coming into the reservation.

I also did a study for John Hopkins at that time to see why our folks weren't getting vaccinated, even though it was having horrendous effects in our tribal communities.

And it was our younger people in that study that said, "We don't trust the government. We don't trust what they're giving us is what we need. We suspect that we are guinea pigs for the government."

So, again, back to that trust, and the effects on closed communities and tribal communities is very prevalent and very systematic, and we have to protect ourselves in ways that are maybe not seen as very healthy, but they're a rudimentary response to an

overwhelming pandemic in our tribal people.

We've been there and done that. We've had smallpox. We've had, you know, all those things that wiped out three-quarters of our tribe. So it was a very traumatic response that you've seen tribes do.

So our tribal communities, almost every tribal community closed their borders. So that is how it can affect health and health outcomes.

MS. SARI: Hi. So for me, I think sort of similarly, "community" means, you know, it's any sort of shared value system, belief system or shared experiences that can tie a group of people together.

And for me that's a lot of things. That's the Iranian American community. That's the transgender or LGBTQ community.

And I think as we communicate and exist within our communities that --sort of, again, building off of what you said, it is this trust, and it is this level of connection that we have with each other that I think is valuable not only in a social and personal

sense, but also when we're talking about things, like healthcare. Yeah.

MS. AMBARDEKAR: Yeah. Just to build off of that too, I think for our young adult patient community, a big thing about trust is people of the same age and the same sort of generation in a lot of ways.

So I think a lot of our community -- like, if we have a parent telling us something -- I think someone earlier said, "Don't tell Gen Z what to do." And I think that rings really true. You can tell them, like, how to think, but not, like, create that forced opinion.

So for my community, it's very much, like, are we of the same age; do we have the same, like, quote/unquote, "vibe"?

And so I think that all plays, like, a huge role in disease management and acceptance and identity formation, particularly when you're young and sick and you don't, you know, see other folks your age having to be part of hospital systems or take lots of

medications, that sort of thing. So yeah,

MS. WILLIAMS: To continue building off this conversation, the work "community" means to me the body of connection. During a very profound conversation I had recently, this person said to me that outside of your mother's womb, the community becomes your womb.

And that resonated with me, because the womb provides a nurturing environment. And if I had to add to that statement, the community should become the body in which we stay connected to be nourished and fed.

A healthy, thriving community means that people should feel a sense of belonging and connected to others who make up this body. So whether it be through relationships or shared experience, where we live, work, and play and even congregate virtually, we have to address this issue of isolation in our communities.

If we think back hundreds of thousands of years ago, communities, tribes, they relied on one

another for survival. And today's America is only widening the gap, and this isolation should definitely be looked at as one of the social determinants of health.

MS. DAVE: To me, I think there's kind of two types of communities. There's one that's already established, you know, based on maybe what medical condition you have or race, ethnicity, things like that.

And then the other community is the one that you build. It's the support system that you build for yourself and the people that, you know, you can rely on or have been in your shoes, and they're the people that will always be there for you.

MS. EPPS: Thank you so much. Actually, then I want to ask a follow-on question about that. LaToya, you mentioned -- I actually had a sidebar earlier with Dr. Kipp talking about isolation -- or a word that Dr. Kipp used was "segregation" of an individual from their community.

Did you all have any comments about

that?

MS. YAO: I think it's really critically important when we look at clinical trials and we're looking at one member of a community that has that disease or that disorder and we remove them -- we extrapolate them from the community to engage in clinical trials, we haven't looked at the collective of that community.

So if you come into the reservation, and you take a child, and you say, "They're going to get clinical trials," but you don't explain to auntie and uncle and the tribe, this is what's going to happen, and this is how they got access; then you've eliminated a sustainability community that they're going to return to.

And I think of Ms. Burgess, to you and your son, and I heard you say that "We got this, but people weren't happy about it for us."

And so, you know, if we're not working with the community around clinical trials, the propensity to sabotage, the propensity to feel like,

"Oh, I'm embarrassed, because I got this and some so and so didn't get it," and to be treated differently by your community -- so if we don't do that community education and that community engagement and let the community know, "This is what's happening," "Here's how you -- here's some education around it; here's a town hall; here's whatever," then to create that understanding for communities that haven't had access historically and have never had access, then you create strengths, you create sustainability, and you created a community to hold those people as they get well.

MS. WILLIAMS: I'll add to that in my introduction, I alluded that I was a pediatric patient, and I had very complex health issues as a child that has followed me into adulthood.

And sadly, the systemic issues that existed for me as a pediatric patient still exists for me as an adult.

I think back to the year 1991. I was all of 13 years old and discovered a breast lump the

size of an egg. And during that timeframe, I also experienced both of my grandmother's passing away from breast cancer just eight months apart.

So that was extremely unusual, and also I look at it as a missed opportunity for my pediatrician and network of providers to discuss the option of considering me for a pediatric trial, as another source of care, and interventions could have happened earlier that may have changed the trajectory of my disease, as I'd later be diagnosed with stage-3 breast cancer as a young adult.

I was misdiagnosed at 29, accurately diagnosed at 30, because I was not being heard, taken seriously, even with my history of finding that breast lump at the age of 13.

And the feeling I remember was how isolated my parents felt -- my family felt. In the early '90s social media didn't exist; the internet did not exist as we know it today, and I wouldn't dare tell my peers at the age of 13 that I just had breast surgery.

So this history has led to me and having this lifelong career in research at a community level. And community-based engagement is only now gaining traction, and few drug developers have the vision and support to support this paradigm shift.

So the innovative work that I do at Inside Edge Consulting Group, I'm leading a team across the country -- boots on the ground, and we're focused at a community level to enhance participation in clinical trials in an intentional way to educate, demystify, and co-create with these communities health solutions that leads to higher enrollment in clinical trials.

MS. DAVE: Yeah, I was just going to add to that and what Dr. Kipp was saying about community engagement and trust building.

I think the way that it's done, at least in our community, needs to come from a lens of peer support and really providing that basis of, like, first, this is a place where you come to support each other and to seek support and to understand your

condition and the way that your identity has shifted with that condition, and then we can talk about things like clinical trials, which feel like very sterile and often long removed topics from the actual everyday experience of being a patient.

So we do six peer support meetings per month at Generation Patient, and we did one, I think, last year focused on clinical trials and just, like, a open discussion about it.

And I think the fact that this group has been meeting -- like, some of them have came for over 300 peer support meetings at this point, but they're able to ask questions in a way that are very much centered on their experience.

And I think that's how you start to build community and to build that trust is not coming in as a lens of, "Here, let's talk about clinical trials," but, "Let's talk about your experience first and get to know you as a person and then talk about trials." So yeah.

MS. WILLIAMS: Just to add on a little

bit to what Sneha said, I think in the pediatric population and our generation, there's a little bit of stigma around, like, talking about chronic medical conditions, and that's when you feel that community is not necessarily there for you, or there's not a sense of trust.

And that's when you kind of start to find a different group of people that are supportive and where there's a little bit less stigma about talking about healthcare conditions.

MS. EPPS: Go ahead, Nasrin.

MS. SARI: I just want to, you know, build off of what everyone else has said around the sort of isolation aspect, where I think especially when you are from a diverse perspective, whether that be an ethnic or racial minority or, you know, gender diverse or of a certain sexual orientation or anything, there's already a level of isolation that you're exposed to within your community.

And then if you have a chronic illness or if you are undergoing any sort of long-term or

short-term treatment that just, it compounds on itself, and it creates really difficult mental health situations for patients who are already having difficulties with their medical health.

MS. EPPS: Well, I would love to ask a follow-on question along those lines. And it's maybe not so eloquently worded, but it has to do with cultural values within a particular community.

And then what I'm hearing, there's some values that may work to be supportive in one particular community identified with, but there may be some that you feel are not supportive for your particular situation from a particular community.

And you belong to not just a single -- I don't think anybody belongs to a single community. So my question is, why is it important for researchers to be aware of these values for a particular community?

And can you maybe give an example of, you know, why this is so important?

MS. KIPP: So I'll start, as you know

from numerous shout outs from Christine, we are the recipients of a REACH contract.

And what we've looked at and what we found is we've looked across several Indian reservations across the United States and our impetus has been to work with tribal colleges, because tribal colleges are the repository for education and any intellectual property within that tribe.

And our early findings -- and actually, we already wrote one article about this, indicate that as native folks, that there are cultural values around blood draws. There's cultural values around taking hair samples and blood samples. There's cultural values around tattoos and different-- this varies among tribe.

And so if we, as interventionists, try to engage a community, we have to be aware that there is going to be some historical trauma related to the medical model of systems.

And we got to put that in perspective. When we look at Indian Country -- now, that's where

I'm going to speak from, is Indian Country is dependent on a socialized medical model called "Indian Health Service."

It was seeded to us from the government for our lands. Remember we got education, health and welfare; right? Oh, yeah, that worked really great.

So we've got the highest disease, lowest college attainment rates, all those things. But the issue is the system has set us up to distrust it, because IHS is severely underfunded.

So it's either life or limb with IHS. There's no intervention. There's no prevention. It's, like, "Are you going to die? Okay. We'll send you out."

I'm working with a tribe now on medical device systems for diabetes, and the tribe told me, "We can't afford it." So here's what we do. We have a committee. If the person is on two insulins, then they might get a medical device. If the person has several emergency room, then they might.

So that's where we're at. We're at the

Hunger Games in Indian Country for good medical care. And we're talking here about intervention for our children for access to clinical trials.

We found that we've got to start at the basic with our people around education, around listening to fears, around helping understand those fears, and then moving forward.

It's imperative that you can't go into a community that has been traumatized by a medical model and say, "Here's some more medical model that we don't know if it's going to work or not."

So that's why we got to develop those paraprofessional pathways. We use a lot of -- we partner with community health workers, promotoras community health -- we call them community health -- to deliver the message, because they're the auntie who sits across the table and tells Grandma, you know, "It's time for you to check your device," and tells the grandkids, "Don't let Grandma have these potato chips"; right?

And so that community model has not

occurred in clinical trials, and that's what we're trying to move forward with our pieces of research is we got to engage the community through community-based, participatory research in an equitable model of service and collaborative care.

MS. SARI: First of all, I have to say I absolutely agree with what was just said.

I think especially in a pediatric space, you have to engage, you know, parents or caregivers or community in a way that is actually meaningful and then there based off of their values.

And values differ across not just different communities, but different sub-sectors within those communities and then different people.

And so when you're, you know, modeling these things, when you're designing a clinical trial, or when you're in a research team and you're trying to understand the values of a group of people, you have to actually get in there and listen to their values.

You can't just say, "Well, we're going to take into consideration the values of what we think

this group believes in," because members of that group are multifaceted. I'm multifaceted.

You might take, you know, me as an example and say, "Okay. This person's ethnic background is from a majority Muslim country, and so you know, this person's values are going to be highly religious," and you know, maybe whatever preconceived notions come along with that.

But then when you come onto my level, my values could differ from whatever your assumptions are. My values could be more based around my experience as a transgender person and, you know, moving through life with that sort of label, especially when it's a highly politicized sort of thing.

And so understanding what that person, on an individual level and then a family level and then a community level -- understanding what the patients have gone through and then understanding where their values come from, I think is really vital, and then using that when you're effectively --

hopefully effectively communicating with their families and communities.

MS. DAVE: I was just really quickly going to add to that too. I think one of the things that we have heard a lot from our community about is the hesitancy to approach topics that can feel very sensitive, like sexual and reproductive health.

And I think even when we're thinking about pediatric patients, these are really important topics to bring up in a way that's sensitive to the individual cultural backgrounds of the person, but also creating room for questions to be asked in a way that doesn't feel, I think, interventional in a bad way -- if that makes sense, anyway, to the family.

So I think that is, like, the biggest thing is that we don't sometimes know how to ask about these things. And so being able to create opportunities for those pathways, but also for explicit discussion of that.

So just really quickly, for example too, we developed a sexual and reproductive health,

like, checklist type of thing for physicians to ask for young adult patients about questions that they might have.

So I think these are really great opportunities to really bring people in and get their questions asked that they might otherwise be scared to.

MS. WILLIAMS: I got to say that I'm really impressed with these young voices on this panel.

The brilliance that they're bringing to this conversation is something that I applaud, because when I think about values and I think about my own family, I had to be that generational curse breaker.

I have two grandmothers that passed from breast cancer, one from the deep south, one from the Caribbean that immigrated to the U.S., and they had the same mindset that we don't talk about disease or the big C in the family.

So they tried to self-medicate until it got to the point they were already at stage-4. It was

too late. And I did not want that for my life, because in my young mind, cancer equaled death.

So I became that voice. I became that outspoken component and representative of my family. I check in with my family. You know, we need to know our family history, especially when it comes to genetic testing.

When I did genetic testing after my diagnosis, I realized beyond my grandmothers, I don't know my family history. I can't tell you what my grandfather passed of. I can't tell you what type of cancer my uncle passed of.

That's not okay, because then that skewed the results of your genetic testing. So we can't be silent about this. Sometimes we have our cultural values, but when it comes to health, we have to be intentional in knowing our family history

MS. DAVE: And just adding on to what the other panelists have said, I think that when the, you know, study investigator or whoever is conducting the clinical trial is aware of these cultural values,

you're able to facilitate that communication better.

And I think it overall improves the experience for everyone, because it's more accommodating, and it makes you feel almost more appreciated for being a part of the trial.

MS. EPPS: Yeah. Can I just say, to add on to just how phenomenal you younger folks, which means everybody up here, you know, compared to me, are on this, is that when you're talking about isolation or talking about where there's sort of uncomfortable subjects, you all are here talking about them, which is huge.

There is, in other realms that I won't go into, people who won't talk about things that need to be talked about, who are a lot older than you are.

So I commend you. I hope you continue. This is not the end of this discussion, but I just want to bring that out, because I think it begs the question, and we were talking about teaching or learning about values, who's going to lead that teaching?

And my suggestion would be folks like you all, because you have the nuances about these things. It's not black and white what a chronic disease at a young age means, what you may or may not choose as a gender or sexual identity means for somebody.

You know, these are things that we old folks maybe -- we just don't get it. So that's what I wanted to say about that.

So moving on along that then, what are steps that institutions -- and I had on my list industry and academic, but I'm going to say a bunch of institutions -- they can be community institutions, such as, you know, churches, synagogues, mosques, you know, institutions, what steps can they take to build and maintain trust between members of a community and researchers, you know, clinical trial folks?

So you all have at it.

MS. KIPP: I think if we used more the community-based participatory research model that has been developed by Dr. Wallerstein and Dr. Isabelle --

and I can't -- her name is failing me, because I've been a practitioner of CBPR ever since going into research, because it's really an equitable model.

If you look at CBPR, it's an equitable model of engaging communities in dialogue around what does this mean to you?

And sometimes it's a basic question of how does culture play? So we've already done this among several tribes around clinical trials in gene therapy.

And what we're finding at this present moment, real-time, is that native folks don't understand clinical trials. They want to know more before they make the decision.

And so what a lot of the tribal colleges have said and tribal leaders have said is we want curriculum, we want people to come to our isolated reservation in whatever part of the country and talk with us about that.

And we want people who look like you, meaning me, because I did the focus group. So those

things are critical, and I'm not trying to be ethnocentric, but our people have to have trust and their levels of trust isn't from the MD and the white coat, because that hasn't worked well for us. Maybe; maybe not.

But it's not removing them too; it's the pairing of them in a relationship base; that this is research, and this is -- we're trying to find out what's best for you; how can that work for you; what won't work?

And we even asked the question, who will you talk to think if you're going to take a clinicals trial? We had medicine people who were concerned about how do clinical trials mesh with our traditional medicines.

These are critical needs that tribal communities ask and need response to, but we need to treat them and be with them. It's not equitable. It's not clinical trials on us. It's clinical trials with us.

And that means us; that means the

researchers; that means the docs; it means the interventionists; we become the "us."

But if you keep saying it's, "Oh, we're bringing this to you as a gift," no, it's about "with us," because we can do that and extrapolate people for a clinical trial, but they have to return to the community.

And the community is the community that will heal them. And so we're leaving out the healing part for our people.

MS. DAVE: I think as a patient, there's a couple things that I would want to see in these with these institutions.

The first one is just transparency, like being transparent about why a test is being done or why a study is being prolonged or shortened and just being kept up to date through, like, standard communication about what's going on, like how's the research data of the study going and maybe, like, an overview of the next steps.

And then I think the other thing, like,

leading into that is facilitating communication and just being informed that a lot of the times in pediatric studies it feels like the investigators or whoever is facilitating the study is talking directly to the parents. And sometimes, like, bypassing the pediatric patient.

So, like, obviously, with taking age group into account for maybe, like, patients above the age of 10 to 12, incorporating them into the conversation with them being the main focus, as opposed to the parents.

And since parents are the ones that are consenting, they obviously have a lot of questions and want to know a lot about the study.

But I think it's also important that the students questions are addressed first, because from personal experience, a lot of times at a healthcare office or at the doctor's office, you know, parents get through their list of questions with the doctor, and by that time it's either, you know, been a while or you forget what the question is.

And so I think it's important to address pediatric questions and concerns, just as much as parents.

MS. SARI: I agree. Absolutely. And I'd say it doesn't even necessarily have to be 10 to 12. I think that at any age a pediatric patient has to be included in that conversation.

And I think beyond that, it has to be an effective language; it has to be communicated in a way that people can understand, whether that pertains to age or preferred language or anything.

It has to be in a way that people can latch onto, and they can really understand what's about to happen, because especially with these clinical trials, it's their lives, and it's their quality of life that is in the hands of these doctors.

And if they don't fully understand what's going on, then that's not truly informed consent, to be honest.

And then beyond that, I think that in terms of building trust, it can't just be about, you

know, going and telling a community what the information is.

That's an important aspect, but it also has to be -- I think it was called "bidirectional" before.

It has to come from both sides, because I think just as important as disseminating accurate information is understanding what that community needs specifically, and then beyond that, taking actual action on it and not just, you know, saying, "Okay; we've heard you," because that's an important first step, but then it's taking action to demonstrate trustworthiness. So yeah.

MS. DAVE: Yeah. And one of the things that I think about with this question for institutions in particular is, are you taking steps to deserve that trust and deserve the engagement?

One of the just personal frustrations that I've had is I really struggle to get access to data. So, like, when I was looking at a multidisciplinary review, I saw a lot of information

redacted.

And whether that's academic-in-confidence, commercial-in-confidence data, that is not my problem to solve. But the problem is, is that as a patient, how am I supposed to trust when information that I want to know is redacted?

How am I supposed to trust when the medication that I'm being a part of for this trial is not affordable? How am I supposed to trust when long-term safety data is not available as a young person who has decades to go through for life?

So I think these are some broader questions that need to be addressed when we're thinking about building diverse populations and clinical trials, especially for the next generation of patients who are going to need this data and need this information.

MS. EPPS: Thank you. Let me ask you a follow-on question on that. When you're talking about bidirectionality and -- or that's a word. So who was it, Dr. Lee, this morning that said, "No more word

clouds"?

But about the patients, you know, taking leads and things, what are areas you consider really important that gives the patients -- well, let me back up for one second.

Let me just say, as a now decades-long pediatrician, I agree 200 percent that a child of any age can tell you what they want or how they feel, even including nonverbal kids.

If they don't trust you, you know it. If they're not happy with it, you know it, whether they can say a word or not.

So, you know, soliciting information from the patient and the parents too. But that's huge. I think people forget that.

But what are sort of really important areas of empowering the patients in this process, and even a pre-question is, when is all this supposed to take place?

When are these activities taking place? As the protocol is being developed? Is this something

to plan for, you know, a couple years from now we'll have stuff in place, so we can have a trial in our area? So those are two questions for you.

MS. KIPP: I think that as we look at the development of research, what we've done -- and I'll just use what we've done as an example, is we've included the tribal colleges in the questions of the focus groups. Will this fit here? Does this work?

And then we did reiterations; huh? So we went back to FDA, and FDA said, well we need to know this. And so we did that community engagement even around the development of the focus group question.

And so those methods of empowerment are really systematic through focus group, but they're relationship based.

So we all know all the docs sitting here that people don't get better unless they believe they're going to get better; right? People don't get better unless the doc has a trusting relationship with that person.

So why is it then that we look at clinical trials and extrapolate, instead of developing those critical relationships? And we don't have to do it.

We have to have people in the community paraprofessionals, community health workers who can also do that and then follow up on assessing did they take their medicine today; did they do this?

But we've got to engage the community in a system that's been very keen on eliminating communities and individualized treatment.

I, as a clinical psychologist, have recognized the need that even in individual therapy, I still will go into the community and provide community information on mental health around depression and anxiety and historical trauma, because the community has to support the movement of wellness in the community.

The World Health Organization defines a healthy community this way. A healthy community is when the health is at the local level. And a local

level means cultural and language level that the local folks can understand. None of the jargon.

I'm going to finish this by honoring my mother and what not to do. My mother died when she was 96 years old. I lived on the reservation for quite a while with my mother, and then I returned to become the tribal college president.

And as she was dying, she had a little file at Indian Health about this thick. And she would get sick, and I would tell her, "Come on, Mom. Let's go to the hospital." And she'd say, "No, Billie, I'm, I'm not going there, because they talk to me like I'm stupid."

And she wouldn't go. So we can't jargon people. We have to talk with them in a language that they can understand. We have to talk with their networks and under language that we understand, and we have to engage the community for better health outcomes.

MS. WILLIAMS: So when it comes to trust, I no longer have blind trust. Defining

conversations is how I seek out trust, accountability, and build connections. And it was a recent visit to my GI doctor, and I realized that I'm still dealing with implicit bias.

I've been seeing this doctor for five years now. We've built a rapport, but I just asked him during my recent visit, I said, "Why haven't you recommended me for a clinical trial?

Is it because the visits are always rushed, or you don't think I would agree to it, or maybe you just don't know enough and how to direct me to towards a trial?"

So, you know, he's a Caucasian man, and he kind of stopped in his tracks, but then said, "You know what, thank you for asking me that question, because it's all of the above."

Then he got excited to tell me about a TED talk that the hospital recently did, and he wanted me to watch the video.

So I want to speak to my non-scientific audience. Allow yourselves to ask questions, give

yourself that permission, because questions are more transforming than answers, and questions, unlike answers, demand that engagement that we need for that transparency.

I don't know if young people say, "I like people to keep it real with me." You know, I want to hear those unpopular answers, because that's how I build trust.

MS. AMBARDEKAR: And just going a little bit to that aspect of where pediatric patients can kind of use their voice, I think kind of giving feedback at every stage in the developmental process of the clinical trial.

You know, asking a focus group of patients that includes ones who might potentially be in that clinical trial, but also ones who would not, and kind of just getting feedback that, you know, "This is a clinical trial. This is why it's being conducted, and this is what it's planned out. There is these tests and these study visits, and how do you think we could make this more comfortable and more

accommodating to the target age group?"

And I think that would help build trust also just knowing from a patient standpoint that my peers have provided feedback and kind of reviewed that study and made it more accommodating for this population.

MS. EPPS: Go ahead.

MS. DAVE: I was just going to say, I said in the previous panel, but I really do think that patients have the ability and capability to be equal contributors to the entire process.

And last year we published eight peer reviewed journals -- or publications, all of which had a young adult patient as a first author and majority were drafted by young adult patients.

So I think there's a real opportunity to shift the way that we think about including patients to really ensure that they have part of the leadership of the trial design, the protocol, and what comes after.

And I think that's a way to get that

integrated feedback of lived experience throughout the cycle and really give ownership, like, "We trust you as an equal partner; we want to give you authorship; we want to give you that same opportunity as we would someone with a PhD or MD," whatever that looks like too.

MS. SARI: Sure. I think a lot of the ideas that have been discussed have been really good. And I specifically want to talk about what Anvita was saying, where it's, like, it has to be throughout every stage. It has to be a consideration from the beginning and from planning the clinical trial.

Because if there's not a space for groups where there typically isn't a space, then how are they supposed to start trusting in these institutions?

And then sort of like LaToya was saying, I think that the transparency aspect and also you, Billie Jo -- yes, sorry -- your name is right there, that the transparency aspect is really vital.

Because if you're using this jargon or

if you're just, you know, throwing around slogans or language that we can't necessarily understand, based off of generational divide or based off of any sort of anything that could cause a difference in language, then trust starts to break down.

Because I think that when we start to hear, you know, slogans, it feels like something is being sold, and I think that when something is being sold, then we're less likely to trust it. So yeah.

MS. EPPS: Wow. So on that, I hope you all took notes, because I think it's pretty much all there, so I'm just going to thank you, the wonderful panel, and pass it on to the next.

My apologies folks. I'm advocating my responsibilities. Let me introduce the next part of the program. And so this is going to be three presenters on best practices that help children and families to stay in clinical trials.

So we'll have Tamorah Lewis who is a chair at Pharmacology and Pharmacogenetics in Hospitals for Sick Children. That's in Toronto, I

believe. Christina Edwards will follow, and she is director of Clinical Trials at the National Minority Quality Forum, and then Puja Umaretiya -- sorry -- I'm going to slay your name, Umaretiya, who is assistant professor in Pediatric Hematology/Oncology at UT Southwestern. Yay, UT.

So I'll let those guys go ahead and -- those ladies take over, and thank you.

MS. LEWIS: Good afternoon, everyone.

So as mentioned, there's three of us who are going to speak in the next 45 minutes and really our goal is to share different perspectives about how to help families start and stay in clinical trials.

So as mentioned, my name's Tamorah Lewis. I'm a physician and a scientist from SickKids in Toronto. And my talk is about strategies to combat structural racism, how we can improve diversity in pediatric clinical trials.

So today, in 15 minutes, I hope we can discuss how structural racism can impede a family's

ability to enroll and to stay in clinical trials and to speak about potential solutions that can help us combat structural racism specifically as a barrier for optimizing clinical trial enrollment and participation.

So I think I'm speaking to the choir here, but it's always helpful late in the day to ground ourselves in why we're here and why this is so important.

So we know that different demographic groups have variations in health outcomes, disease prevalence, and response to our treatments. And by increasing diversity in our trials, we can better understand these variations and develop healthcare interventions that are more effective and equitable for all patient groups.

In addition, when our clinical trials are diverse, we know that our results are more generalizable. The results may not be applicable or safe for all groups if these different groups are not enrolled in the original clinical trials.

And lastly, clinical trials can be a mechanism to identify disparities. So if we don't have diversity in our clinical trials, we don't understand differential efficacy or differential safety signals that can be crucial for developing more targeted interventions in the future.

We know that drug metabolism, drug side effects, and drug treatment response can vary among different racial and ethnic groups.

So if we don't have adequate representation in our trials, we won't know how efficacy and safety differ by specific populations. And a diverse study population can enhance the robustness and reliability of our research findings.

And very importantly, based on the panel that we just heard, you know, we have a duty to enhance public trust, so patients are aware of differential ability to enroll in clinical trials and differential ability to stay on clinical trial protocols.

And we as a research community really

have the burden to repair the mistrust that marginalized communities feel. And building this trust is crucial for recruiting participants and conducting ethical research.

So now we're going to talk specifically about structural racism. And when we think about structural racism, really another word for this is structural disadvantage.

So we know that certain racial ethnic and other marginalized groups in the United States experience different ways that resources are distributed. There's different ways that people relate to each other, both on an institutional level and an interpersonal level.

There's clear variation in who has power, and this plays out in how institution are organized, which patient populations are prioritized, and the type of medical care that families have access to.

And this table from the Kaiser Family Foundation really does a great job outlining all the

social and economic factors that drive differential health outcomes. But more importantly, I think can also drive research participation.

So we know that families from different backgrounds have different levels of economic stability, neighborhood and physical environments, education and food resources, community and social context, and healthcare systems that can all affect medical outcomes, but really importantly affect a family's ability to participate in research.

And I've outlined and read some of the things that I think are most important to consider when scientists partner with communities to design clinical trials.

So a research team that is truly invested in diversity in clinical trials will actually take the time upfront at the time of early community engagement and at the time of protocol development to explicitly address each of these different columns and explicitly try to understand how their target clinical trial participants might be affected by these factors

and what they can do in their protocol design to actually mitigate some of these barriers.

And we know that societal disadvantage affects families in many different ways. And I'm just going to show you three very simple graphics that beg us to ask ourselves the question, do all families have equal opportunity to show up at our clinical trial sites with adequate emotional and cognitive bandwidth ready to engage in complex research related discussions?

So we have to take a moment and think about a family's lived experience outside of the walls of the hospital, outside of the walls of the clinic. And then imagine how that lived experience and the differential lived experience affects their ability to come and sit and engage with you to discuss a consent form or to discuss a clinical trial protocol.

So this figure on the left shows what many of you might already know, that income and wealth varies significantly among different racial and ethnic backgrounds in the United States.

And you can imagine how a family that is growing through chronic financial stress is in a very different situation to consider enrolling their child in a clinical trial than a family with relative wealth.

We also know that different racialized groups face social injustices, such as incarceration, at very different rates.

So if a community is in chronic crisis, because, let's say, the men and boys from their community are being arrested in incarcerated, that affects a family's ability to show up, ready to discuss clinical trials.

And we also know that different racialized groups experience gun violence and death by gun violence at very different rates.

And so these are just three very basic examples where we have stark data of differential lived experience by race and ethnicity in the United States and how if we're going to try to, quote/unquote, "Conduct diverse clinical trials"

without thinking deeply about these topics and engaging with these topics and understanding where families are coming from when they walk through our clinic doors, we're going to have trouble with success.

So now, we'll talk specifically about some solutions for clinical research, diversity, and equity.

This is a wonderful paper published in 2023. The name of the paper is at the top of the slide. And we're going to tackle two big topics from this paper, which are barriers to clinical trial participation and solutions.

The first barrier is limited access to healthcare, and this is a very major barrier that can affect clinical trial recruitment and differential access to basic healthcare, as mentioned in the prior panel, really can disproportionately impact racial and ethnic minority groups.

So this figure is from a website called milkeninstitute.gov, and the on this website you can

search by different disease status and look at the density of clinical trial sites across the United States. And this is an example where I just typed in sickle cell disease.

So we know that limited access to healthcare disproportionately affects racial and ethnic minorities and can be a major hindrance to their enrollment in clinical trials.

Research sites are often distant from the most minoritized and marginalized populations, making participation very difficult due to basic things, such as transportation challenges and having to navigate very unfamiliar locations.

In addition, we know that people who have limited financial resources can really have insurmountable caregiver burdens. So caregivers from racial and ethnic minority groups may face additional challenges in participating, because they can't get out of elder care or childcare responsibilities.

And also, racialized and rural individuals may be in more service-intensive or labor-

intensive occupations with limited paid time off.

So as opposed to someone like myself who has the luxury of taking a day or two off each month to participate in a clinical trial, another person may miss an entire day of pay and not be able to feed their family if they decide to participate in a clinical trial.

So what are some tangible solutions? And these are the things that we have to consider when we actually design our budgets for our clinical trials, because if you haven't budgeted for these solutions, you are not going to be able to enroll participants who face these barriers.

And so it really takes intentionality and planning upfront. So how are we going to include incentives and compensation in our budgets at the institutional level?

So we know that financial remuneration and reimbursements, just for study-related lost resources, can really help bolster families and their ability to weather the financial stress of clinical

trial participation.

Transportation support. So you know, actually doing something very tangible, like Lyft vouchers or Uber vouchers or having -- you know, if you're getting multiple patients from a certain rural community, having structured transportation plans to bring them to clinical trial sites can help address transportation-related barriers.

Childcare and elder-care support. So you know, I think a lot of times research teams think about these things in theory or in an abstract way, but if you really want to enroll families with increased caregiver burden, you actually have to budget for how you're going to help them provide care for family members when they bring their patient for clinical trial site visits.

And also, how can we take clinical trial conduct out into community-based clinics? So if we place our research clinics in community-based ambulatory primary care offices, that can both allow easier geographic access, but also allow patients to

engage in clinical research in a site that feels comfortable and less intimidating.

And lastly, flexible timing. So we know that our clinical trial visits are really timed around convenience for physicians and researchers.

And so if we want to allow families to participate who have the types of jobs where they can't miss work, we really have to get creative about flexible timing, allowing evening and weekend research-related activities or virtual activities that don't force families to miss so much time from work.

And this figure is from a company that works to improve research diversity. And you can see on the horizontal access different ways that research participants learn about different research opportunities.

And patients from different racial backgrounds actually report very different ways that they first learn about research. So an important part of diversity is using non-traditional or alternative routes to advertise your clinical trial that might

allow different research participants to learn about it.

So taking extra caution when we develop eligibility criteria is a key step. Are we functionally excluding certain patient groups because of the way our protocols are designed?

And then also we heard today about decentralized trials. What study procedures can we perform remotely? And are there easy to reach community sites where we can conduct certain study procedures?

We're next going to talk about racism as a barrier. So complex issues surrounding perceived interpersonal, institutional, and structural racism serve as a major obstacle to recruitment of racialized groups.

And we know, based on many conversations today, that lack of trust in the medical and scientific community affects racialized patients.

There have been historical abuses and in some situations there are ongoing abuses of

racialized communities, both in residential schools and nutritional research, other types of examples that lead to this deep seated mistrust trust.

There's explainable and very understandable fear of experimentation, present day discrimination that racialized families experience in their day-to-day encounters with the medical system.

And we know that there are worse health outcomes for racialized communities. And importantly, patients from racialized communities also know this critical fact.

And so all of these examples of the effect of racism really can affect a family's ability to enroll in clinical trials.

This study is in adult transplant patients, and they ask transplant patients their experience of medical racism.

And you can see that there are big differences in the way African American patients and white patients respond to these questions like doctors treat African American and white patients the same.

And you'd better be cautious when you decide which healthcare organizations to trust your family with. And patients sometimes can be deceived or misled by healthcare organizations.

So these are, you know, patient responses and patient experiences of their medical care. So you can imagine if patients are having these worries about their medical care, it can affect their ability to engage with research.

So we're getting to my last slides and these are just examples of how to address racism barriers. And I think a very important one that's come up today is this concept of historical trauma and educating research teams about cultural and historical trauma.

So if a family comes to you and you can only speak to them in a way that you would speak to the most privileged family -- you know, you cannot engage with them about their cultural history with medicine -- you don't feel comfortable talking about issues of mistrust, you're really going to have a

tough time for your research coordinators and your research team to enroll diverse participants.

And so I loved how the panel talked about values and how cultural values can be so personal. And so what we don't want to do is go and say, "Talk to all black patients this way. Talk to all LGBTQ patients this way."

We want to teach our research teams to actually have deep cultural humility. So when you approach a family, you spend time saying, "What's important? What are values important to your family? In your culture, what are some barriers that might make research scary? What are some values in your culture that might make research exciting?"

And spend the time and have that cultural humility, and the research team is not fearful of engaging in those conversations.

So to conclude, structural racism and structural disadvantage undoubtedly impede research entry and participation for many racialized families.

And a study team that's committed to

diversity actually will not talk about these things in a theoretical sense, but actually sit and focus and talk about practical ways that they're going to address these barriers before clinical trial launch.

And in the two talks that are going to follow me, we're going to talk about inclusivity best practices from a nonprofit research lens, and also how do we improve diversity in vulnerable pediatric groups such as oncology clinical trials.

Thank you.

MS. EDWARDS: Okay. Good afternoon, everyone. My name is Christina Edwards. I'll be talking about continuing the conversation from what Tamorah discussed on best practices that help children and families to stay in clinical trials.

Again, from the nonprofit perspective, I personally work as a director of Clinical Trials in our Center for Clinical and Social Research with NMQF being a health research, education, and advocacy organization.

No conflicts of interest here.

So we're going to first take a look at these two diagrams here. So on our left, we have our U.S. demographics from 2020. And on the right, we have a clinical trial participation statistics.

So you see here on the left, from the 2020 census, the largest blue image here, we have 60 percent of the U.S. white population.

While you see on the right, they do account for 80 percent of clinical trial participants. Moving clockwise, we see 13 percent of the black population according to the 2020 census. And they only account for 10 percent of clinical trial participants.

Moving up that, you see a huge discrepancy again in our 19 percent Hispanic Latinx community, only accounting for 6 percent of the population.

So that's just a very quick look at some of the disparities that we see generally in clinical trials.

Here we have another diagram taking a

look at the multi-level barriers to clinical research. I'll go through this real quickly. You heard a lot of these throughout the day to day, but on the individual level, some of the issues that come up is time, resource constraints, language, interpersonal attitudes and police of patient and provider, bias, mistrust, lack of awareness and engagement.

Institutional, again, lack of trust, competing goals, eligibility criteria. On the policy, you see here funding mechanisms, accountability, and support for BIPOC investigators.

So I'm going to talk a little bit -- on a high level, three approaches, starting with community engagement and working with some of these best practices on the community engagement level.

So how you engage with the community, depending on the population that you are entering, it can have a pretty determinant factor in the success that you will have in that study with respect to that population.

So for starters, you want to -- you

industry, the sponsor, whoever is bringing their trial, you want to conduct outreach and engage your community-based organizations, advocacy groups, community leaders to gain buy-in, to gain their trust of the community.

So for starters, evaluate the needs of community. What may be publicly available, something like a community needs assessment, you can maybe start there, but you more so want to actually speak with the community, conduct educational seminars, host events.

What that may look like, there's health fairs; there's drives; there's toy drives; there's clothes drives. It will be centered on the needs of the community.

And on the basis of those findings that you have during these town halls against seminars, you gain additional insight into the issues that they're having, into the comorbidities that they're dealing with, into the care options, and, of course, you'll also use these spaces to spread information on clinical trials.

Again, you want to liaise with trusted community members. Who are the figureheads? You want to utilize their support, endorsement to help bridge the gap between the sponsor and the community, and, again, partner with organizations already doing the work.

You won't be the first trying to get into the community. There's going to be people there who have been on the ground and putting in the work to develop their own mechanism -- their own relationships that they have.

So seek those out. Seek those partners out. See what they're doing. It's not always necessary to start from scratch. Amend and tailor, you know, what you need to do, of course, to what has already been done. See how you can build upon that.

And lastly, what you see here is have a dedicated team. When you place yourselves in these communities, it is nice to, you know, not have a round robin of people.

If you have a team that's going into a

community, have a set team. Maybe a team may not be in in the budget. Have a particular contact person. So when you meet with these trusted community members, when you partner with these organizations, you have a point of contact that they have that they can call to, that they can trust when they reach out to you.

So essentially, you form a coalition when you go into these communities. You have researchers. You have these various stakeholders. You'll have physicians as well. You'll have the industry perspective, and then, you know, you'll eventually form that type of relationship.

And it should be longstanding. It should go beyond your initiative. It should go beyond your program. It should be ongoing. Before a trial, before any of that is started, you want to make your presence known.

So at NMQF, we have a few programs, one of them with our Center for Sustainable Health Equity and Engagement.

So with promoting health equity through

education and clinicians and community leaders, we focus on clinician engagement and community engagement.

So clinical teams, pharmacists, partner with SHC to implement QI in community engagement projects in underserved communities.

And then we also have community engagement partnerships with churches, barber shops, and hair salons around the community -- around the country -- excuse me, to engage, educate, and connect people of color to health and social services.

So these are the names for those that I just mentioned, our Faith Health Alliance, our Wellness Warriors, and our Community Pharmacists.

Faith Health Alliance deals with deals with faith health leaders, Hair Wellness Warriors, barbershops, hairdressers.

Essentially we train these people. We educate them. We speak with them. We meet with them. We form relationships with them. And then they, essentially, in their line of business, they go out,

and they disseminate the information to their patrons.

So it may not -- the information doesn't always have to come from you. You know, work with who is already in line and who they would be susceptible to listen to

Just a quick image of where we are.

So a little more community engagement. Ensure the use of culturally tailored education. Again, something we've heard all throughout the day, communities are incredibly nuanced.

You want to be sure to be culturally sensitive. One community is not the same, you know, within one given language, just multiple dialects. Just be cognizant of that and what's going on.

Could tailor customized materials in disengagement in your outreach, advertising and recruitment materials, including social media; marketing and outreach should be tailored to your targeted community.

And then optimizing study teams. So working with community is not only on the clinical

participant side. It also means the research team, the investigator, the physicians that you'll engage, where you'll choose to put your studies, the site you'll choose, who will be the PIs on your study.

So you want to ensure -- well, I don't know if you can ensure. You want to do your best to have the principal investigators, the study staff, they should represent the population of people that you want to eventually enroll.

If we're going for diverse and inclusivity, it is nice when the people that you seek your care from are reflective of you.

Another initiative that we have ongoing at the National Minority Quality Forum in a collaboration with Biogen, so we developed the clinical trial learning community model to identify and mitigate disparities in clinical research.

So the model has been working directly with medical professionals to expand their knowledge on cultural competency and the importance of clinical research via virtual training modules and community

town halls and educational sessions.

I think, again, someone spoke earlier that it shouldn't be assumed that the physician is privy to clinical trials and what that it all entails.

Of course, you know, they're a doctor, you know, but they might not participate in research since, like, residency or fellowship. They still need training or understanding on how to present clinical trials to their patients.

So next, after community engagement, we have effective communication practices. Again, communication style and preferences will vary by family.

We talked about the informed consent process as being such a pivotal time point. And during these times, you want to allocate additional time for participants during visits, especially during enrollment.

Many moons ago, as a clinical research coordinator, you often didn't get someone to enroll on the first time you presented the study to them. And

so working in pediatrics, they're going to take that consent form home; they're going to show it to their family; they're going to highlight; they're going to have questions, and allow that.

You know, you shouldn't put pressure on them. You want to ensure where translation services are needed, utilize interpreters and translated documents. Ideally, all study materials should be in the participant's language.

I know if you're able to have study staff that are able to communicate in the language, that's always great. Utilizing interpreters can be, in real-time, a little difficult, you know. It's often over the phone. But where you can, make it work.

And then communicating trial details, it should be effectively conveyed for total understanding -- study purpose, requirements, benefits.

Benefits are pretty important. You want to -- you know, is there immediate benefit? What

do they get out of this in the moment? Is it more long term? Is it more for people who suffer with my disease, but I won't see any many immediate benefit, but people will after me? So you want to make sure you properly convey that to the family.

During the trial, be available and accessible. This helps to build trust and relationships. You know, you will have to go the extra mile. You know, it's not an adult trial. You're dealing with family, and family is very complex.

So reassure families you are available for questions and concerns. This may include coming earlier, coming later, but keeping an open line of communication.

And as one of our patient advocates said earlier today, "Keep them in the know"; share results and achievements with families. Of course, where allowed, inform families of study progress or any stages -- or any changes, excuse me, and keeping continuous communication; conduct outreach during

visits.

So our next approach here, community engagement, effective communication. We have comprehensive care. So when we say comprehensive care, we're thinking holistic support for the participant -- for the child.

Tamorah touched on this a little bit, but there are going to be barriers; there are going to be issues that the family is facing.

So you just want to be cognizant of these different challenges that they're facing. And while it's not directly study related, it's going to impact retention; it's going to impact how they're able to navigate the study. So take that all into account.

A lot of these -- and with taking this into account, again, as Tamorah mentioned, it's going to require a budget. So when planning, when development on the site side, make sure you negotiate for that.

You know your patients, you know what

they will need. Take all that into consideration.

Incentives, as simple as put, monetary incentives should align with time and effort required of participant and family.

But as you heard earlier, while it may just be a one-hour visit in your office, you don't know what that family took to get there. So always keep that in in mind.

You know, it should be reflected of time and effort. You have to worry about fair market value. But when putting it in your budget, when negotiating, push it to the limit, and make sure that you know families and the participants, they get what they deserve for participating in your trial.

Should be easily redeemable. We used to give cash. Most people don't keep cash in their research sites anymore. It's usually a ClinCard or a gift card of some sort.

But even the assumption that, depending on the community, that they know how to use that, you know, or if they go to an ATM, there's an admin. fee,

so they don't necessarily get their full compensation, because a part of that was taken out.

All that just should be considered when trying to -- when issuing incentives. And consider alternative incentives where applicable, when available, of course.

Institution policy may kind of knock that down. But be creative, and see what you can do and make sure it aligns with their needs.

I think it's my last slide here. So again, with comprehensive care, patient navigation with respect to budget -- it's a budget question as well.

I think many people don't necessarily put patient navigator, social worker, or case worker into their budget. Oftentimes, while it may not be under that label, your clinical research coordinator is going to be doing that.

So if you can, get that put in to your study budget; it works. And with comprehensive care, just considering the participant's full health. It's

on a spectrum outside of disease indication that they have come in for; you have to consider everything else outside of that, and that is going to impact them.

So when they know that, there's a plan for them, they know there's a continuum of care; they know what's going to happen post this study, especially if they have a chronic disease; the trial is working; everything is going great; what's going to happen when this is over.

So when they know that, you know, there's a plan for them -- there's a plan for their healthcare, keep them in the know of that, so there's less angst surrounding that.

And if you, the research carrier -- if you're just a research side or maybe you are in a larger academic institution, be prepared to refer or coordinate those services. Yeah. Again, just make sure you have some post-trial plans and options available.

And that's it. So we covered community engagement, having effective communication, and

continuum of care, comprehensive care, just a holistic look at the participants and their families for consideration when working with them and trying to increase your retention rate and get value out of their participation.

MS. UMARETIYA: Hi, everyone. I am Puja Umaretiya. I'm a pediatric oncologist at the University of Texas Southwestern Medical Center.

And I just want to say how exciting it's been to be a part of this stay and to hear so many perspectives and to be a part of this shared cause to advance clinical trial equity. I'm going to be talking about it from my lens as a pediatric oncologist.

I have no disclosures.

So we've heard this echoed over and over, over the course of the day, so I won't belabor it, but enhancing and maintaining trial diversity is a priority for all of us.

I want to use pediatric oncology in some of my work as a case study really to examine

frontline clinical trial enrollment and participation by race, ethnicity, and poverty status to amplify the experiences of black and Hispanic parents regarding research participation in oncology and then really to focus on our group's work targeting social determinants of health in the same manner and with the same rigor that we used to design drug trials and to hopefully inspire all of us to think about how we can begin to do this alongside our therapeutic trials.

So we've heard about the multiple places along the clinical trial pipeline where inequities can arise. I want to acknowledge that my work really focuses on the later part of this pathway, and that is because in pediatric oncology that's a rare diagnosis or rare disease.

The majority of children with cancer in the United States will receive care at a tertiary center and at one of the 190 COG centers, the Children's Oncology Group, which is a cooperative group that runs our clinical trials, and so most children in the United States with cancer will already

have access to a center with clinical trial options.

And so one of the first things that I wanted to do is really look at who enrolls on clinical trials in pediatric oncology, and specifically looking at a population of patients with high risk neuroblastoma, the most common extra cranial solid tumor in pediatrics.

We looked among a cohort of children who were enrolled in neurobiology study, which captures most, we think, of the children in the United States with neuroblastoma who goes on to enroll on a frontline clinical trial.

And we looked by race and ethnicity -- of trial collected race and ethnicity, and then we used a series of proxy socioeconomic status measures.

We looked at household poverty, which we defined as public insurance only. We looked at area poverty, which we defined as those living in ZIP codes were greater than 20 percent of the population lives below the federal poverty line. And we looked at urban and rural again using ZIP code linked

measures.

And what we found in what you see here on these graphs is that there was virtually no significant difference in enrollment to frontline therapeutic trials by race, ethnicity, or proxy to SES and that somewhere between 35 to 40 percent of children enroll on frontline therapeutic trials.

We then leveraged this data set to look at who discontinues trial participation; getting at this idea of is participation on clinical trials too burdensome for particular populations?

And so we looked at specifically trial withdrawal for reasons other than disease progression and, again, looked by race, ethnicity, and our proxy SES measures and found that while nearly 40 percent of children discontinue participation on their frontline clinical trial, that this did not significantly vary by race, ethnicity, or our proxy to SES measures.

And as we've heard many times today, you know, while this doesn't suggest that there are significant disparities in who enrolls on clinical

trial or continues to participate on clinical trials, this isn't the full story.

And so what I really wanted to do was to understand the experiences of parents from those communities who have been historically excluded or marginalized in our academic communities.

And so I conducted a single center mixed-method study in Boston at the Dana-Farber to understand black and Hispanic parent perspectives regarding clinical trial and research participation, and specifically focusing on barriers and facilitators.

We used some of the recruitment strategies that you've heard already today, really focused on trust, transparency, and minimizing burden to enroll a cohort of 60 parents.

We had a 94-percent participation rate, 100 percent of parents completed participation, and we had 98 percent complete data, and we enrolled this cohort in 3 months.

And I just want to share a few of those

perspectives. So when we asked parents about their perceptions of research and clinical trials, we heard that research and clinical trials are experiments, that research and clinical trials are a way to advanced medicine. And for many of these parents, they were both of these things at the same time.

And so this mother said to us, "For me, clinical trial, I can't help but think of, like, experiment for some reason, because, I mean, it's something that's new and being done to learn about something.

So for me, the word would be experiment. That's what would automatically come to mind, but not, like, in a bad way; in a good way to learn and hopefully advance in the treatment of whatever they're trying to learn about."

When we probed on motivations for participating in research and clinical trials, we heard that they were motivated to access novel or the most advanced therapies to have an opportunity for decreased toxicity to improve care for future patients

and families. And we've heard these themes over the course of today.

But a unique theme that we heard was really to represent the experiences of black and Hispanic patients. And so this mother went on to say, "The majority of research probably involves Caucasians, but I want to provide people with, like, an aspect from an African American family, because it's not -- there aren't as many."

And when we probed on hesitations for participating in research and clinical trials, we heard again things that have been echoed today, fear of the unknown, particularly efficacy and side effects, a desire to protect their child from unnecessary treatments and tests, and then we heard a theme that has also come up today, the history of maltreatment of black and Hispanic patients in research.

And this father of a child with leukemia said, "As a black culture, we were test dummies. A lot of things were done to us in the

hospitals, just to get a better understanding of our race and culture. Some we were aware of, and some that was just -- it was forced upon us. For me, as a black man, having those things done to my ancestors over time, I think when I had first heard about clinical trials, I'm like, no, thank you.

But I think with the understanding that it was happening to my child and that we needed to gather and get more information, I agreed more so to advance her treatment and her care." And he went on to enroll his child on our frontline trial for pediatric leukemia.

As we were designing this study -- as we were thinking about our a priori hypotheses about barriers to participation, something that has come up a lot today was distrust.

We measured this quantitatively and qualitatively in our interviews, quantitatively using the trust in the oncologist scale, a series of questions with a Likert scale, where 1 is no trust and 5 is complete trust.

And our mean was 4.6 in this population, indicating near complete trust. That's not to say that there aren't real reasons for mistrust and distrust, but I'll talk a little bit about some of the things that engender trust in this population.

The second, which we've heard also today, was that information sharing would be a challenge.

And this father told us, "As the parent, finding out that your kid has cancer, you're asked to read, even with all of the threats that are going on at that moment, you have basically a 24 hour time limit to read all the paperwork, possibly do your own research, in order to make a decision that affects your child's life, and you've got an hour to do so."

And I think that speaks to a lot of the limitations in pediatric oncology where we are sharing with a family that their child has cancer and then expecting them to make these decisions in this pressured time.

And I think there have been a lot of

great ideas today about how we can improve this informed consent process that we need to think about in pediatric oncology.

And then our third hypothesis about barriers was unmet social needs. And as you can see here, 73 percent of this cohort reported an unmet social need in transportation, utilities, housing, or food -- about a quarter in transportation and utilities; about half had housing insecurity, and 40 percent had food insecurity.

And this causes a lot of stress during the experience of caring for a child with cancer. This mom told us, "Or you can have a family like mine, where it's a struggle for everything.

Extra visits for a clinical trial would be a lot more added to my plate. But then at the same time, if I'm thinking about my child, if this is something that is going to help him, I'll find a way. But will it cause more stress?"

And I think we've heard a lot today about potentially innovative ways we can decrease the

burden of trial participation for our families.

And so I want to caveat some of this data, because pediatric cancer is really rare. And I think in the face of something that is life-threatening, like pediatric cancer, families really are willing to do anything and everything for their child. So I'm not saying that all of this can be extrapolated to other contexts.

And I think that in pediatric oncology, we have the privilege of being able to build longitudinal relationships with our families that are quite intimate and allow us to engender trust in a way that may not also be able to be extrapolated to other settings.

But at the same time, I think that this data suggests that relatively equitable trial participation is achievable and that distress should not be used as an excuse for underrepresentation.

I think that we've heard a lot of ideas today about how we can engender trust and how we, as academic institutions, can begin to be more

trustworthy so that families are wanting to engage and participate in clinical trials.

And I think some of the data that I shared from the parents in our study suggests that parents really want to have these conversations with us and that information sharing and unmet social needs are real barriers that can impact enrollment and retention.

So for the last portion of my presentation, I really want to focus on this concept of unmet social needs, which is where my research is.

We know that measuring social determinants of health and social needs are feasible across the cancer trajectory. We know that one in three children with cancer at diagnosis has an unmet social need.

I presented data that shows that three of four black and Hispanic families have unmet social needs during cancer care, where they have access to resource specialists and social workers at our tertiary care centers.

And I think this is, in part, related to some of the structural racism and structural disadvantage that Tamorah brought up, and that at the time of advanced cancer relapse or progression, one in two children with cancer has an unmet social need. And I think this speaks to financial toxicity that accumulates over the course of cancer and care.

In our group, we've demonstrated that it's feasible to actually embed these types of questionnaires in our clinical trials. And we've now embedded these in multiple frontline national clinical trials.

We've completed thousands of these surveys with a greater than 85 percent consent rate, a greater than 85 percent completion rate, and less than 2 percent missing data.

And I think when we think about data equity, these data are more specific and potential drivers of inequities in a way that proxy measures of SES or race and ethnicity really are not.

And now, in our group, we're working on

targeting social determinants of health in the same way that we target molecular operations in pediatric cancer.

And so we have designed in work -- really primarily led by the woman at the top, Dr. Kira Bona, one of my research mentors, and two of our colleagues, Rahela Aziz-Bose and Colleen Kelly, we've designed a series of interventions targeting unmet social needs and social determinants of health.

So I'll just briefly speak to them, just to provide insight into the types of things that I think are feasible in this context.

So PD Care is an intervention that centrally delivers groceries and transportations to low-income families at the time of a new child cancer diagnosis for six months.

And this is an intervention that has undergone pilot testing, feasibility testing across two centers, and now is embedded in a Phase 3 trial for pediatric leukemia through the Dana-Farber consortia across 8 sites.

Pediatric RISE is an unrestricted cash transfer intervention, again, for low-income families with either a new cancer diagnosis or a diagnosis of advanced cancer.

This is a six-month intervention that's undergone a single center pilot and is undergoing a two-center randomized feasibility study.

CHEF is a intervention that provides meal kits and assisted nutrition benefits enrollment. This is for families with food insecurity in the first year after cancer therapy. And this is something that's undergone a pilot study.

And then as Assist is our newest intervention. This is a means tested benefits navigator intervention for low-income families at the time of a cancer diagnosis. The idea is for it to provide support for 12 months. And we are planning a pilot study this fall.

At the same time, we heard that information sharing was a challenge. And so I want to amplify the work of Dr. Paula Aristizabal at UCSD, who

has designed a cultural and linguistic clinical trial peer navigator to assist with the informed consent process and has demonstrated improved comprehension of trial components for families who are Hispanic or speak a language other than English. And this is undergoing a multicenter RCT across four centers in the country.

And what I want to leave us with, I think is the question that we've been wrestling with all day today, which is what is good enough?

And in pediatric oncology -- this goes back to our neuroblastoma data, on the left is a graph showing survival curves, where the red is children who don't have household poverty, and blue is children who do have household poverty exposure, meaning that they have public insurance. And you can see that survival curve is not the same.

On the right is children with high-risk neuroblastoma with data disaggregated by race and ethnicity. The green line is children who are non-Hispanic white; the red line is children who are

Hispanic. The blue line is children who are non-Hispanic black. And you can see that those survival curves are not the same either.

And so even when children have access to clinical trials and are receiving the same standardized therapies, our survival is not the same.

And so I would argue that we will be good enough when those survival curves are all the same, and we are not there yet.

And so, you know, I think equitable trial participation is achievable, but this is just the first step to ensuring equitable outcomes.

And I think that things like social determinants of health measurement and interventions targeting social determinants of health are both feasible, may work on improving some of these outcome inequities, and hopefully can be embedded alongside our drug clinical trials.

MS. EPPS: Okay, you all. Hopefully we're going to finish strong. If I can have the panelists -- we've got our big panel.

At the beginning of our meeting Dr. Fienkeng talked about it takes a village. So we're bringing the whole village up for this last panel discussion. So whoever is still with us and wants to participate on the panel, come on up.

In the meantime, I wanted to say thank you so much to Dr. Lewis, to Ms. Edwards and Dr. Umaretiya. Really great presentations.

Just so it's not a commentary on our company, but Dr. Kipp is going to have to leave early for her travel. So she is going to participate in part of the panel, but not the whole panel.

Do we need more chairs up here, or are we okay?

UNIDENTIFIED SPEAKER 7: We're good.

MS. EPPS: Okay. So I'm going to let Dr. Kipp lead us off on the questions.

MS. KIPP: Okay. So we want to thank our esteemed panelists, which there are many today.

And so what we're wanting to discuss is, as you know, best practices that how do we sustain

our children in clinical trials? And we've heard a number of things. So this is kind of our "What have you learned today from this"?

And so I'll start with the first question. Is there something you've learned from today's gathering that you'll bring back to your family or community as a best practice?

And so I'll just -- whoever wants to start, start. You're all very dignified.

MS. YAO: Actually, can we have --

MS. KIPP: Go ahead.

MS. YAO: There is one person I think who hasn't presented or spoken.

MS. KIPP: Okay. Go ahead.

MS. YAO: So we'll start with it, which is Dr. Melissa Penn, and then anybody else after that.

MS. KIPP: Okay. Thank you.

MS. PENN: Oh, the "on" button. And now -- okay. Great. Well, thank you. Thank you so much. It's been a really tremendous day. A lot of learnings.

So my name is Melissa Penn. I work at Bayer. My role is patient engagement R&D. So I get the privilege of thinking about how do we get early, meaningful, and continuous input from patients along the entire research process. And I believe that patient engagement is inextricable with diversity and representation.

My background is as a lawyer and in public health. And for the ten years before I got to Bayer, I founded and ran a nonprofit in rare disease, and I am a rare disease mom.

And through that and continuously today, I look at this through the lens of nothing about us without us, but in the takeaways -- so many good takeaways, I love iCAN. I love what you said.

And I think about -- I thought it was really interesting, actually, that adolescents were saying that altruism was one important reason to participate. And that was -- I mean, it makes sense, but it was still eye-opening.

I loved the comment, "Hey, if you don't

think it's important, maybe it's not the right job for you." And then I'm going to take away Bella, the "Yes, and." I just want to work in that model.

MS. EPPS: Anyone else want to answer that question? What will you take with you today as a best practice?

MS. OGUNO: I can speak from an industry perspective, is looking at the wider opportunity, in terms of the data that we collect.

Do we need to collect ten blood samples versus three; right? Do we need to collect all this information? Not just because we can, but what is the impact? What are we testing? What is the answer that we're looking for?

And I think one of the patient panelists brought a good point, how do we bring the information back; right?

Because as an industry, we're thinking from a competitive perspective. So we black a lot of the things out. We don't want others to know. We just want to have that information until it's ready to

be shared publicly.

But from a patient perspective, how do we share that data back, so they can take that and that continues to empower their journey as a patient and have that information to take back with them to make more empowered decisions?

So how do we bridge that gap, in terms of the data being available?

MS. KIPP: Thank you. Please remember to turn your microphone off at the end. Thank you.

Anyone else want to mention what they're taking back from here today?

MS. WILLIAMS: Sure.

MS. KIPP: Thank you, LaToya.

So I think the biggest takeaway is that boots on the ground must be a part of the clinical trial process.

We need to look at our communities, not as the problems that they have, but more so of the assets and possibilities they can bring to this process.

I loved what I witnessed in Christina's presentation, that she's working with the faith-based communities and pharmacists. And, you know, they have communities that are far reaching that, you know, we can't touch from a lab or from behind our desk.

So I would say when working with communities, move at the speed of trust, anchor ourselves in outcomes, and definitely remain boots on the ground. That's one takeaway.

The other takeaway is around AI. We need to find a way to build that, to make it convenient, not just for researchers, but for providers and community members as well.

When I think about providers, they too need the education on how to make an effective recommendation. Let's make it easier for them on how to connect people to a trial that they're eligible for.

So when I think of AI, I think of how do we make it convenient? Amazon sells convenience. Nike sells motivation. Disney sells dreams. So I

think we really need to look at AI and convenience in that space.

MS. EPPS: Thank you. So -- thank you. Please.

MS. YAO: Hi, Lynne Yao, FDA. So I think the biggest overall takeaway for me today is, like we've said at different times during our sort of, you know, adventure in developing therapeutics for children that, you know, we used to say, "Oh, just do any research, and that's better than nothing."

And then we said, "Well, you know, regulatory-grade research, you know, incorporating standards, like clear endpoints, interpretable data, like, that's all good research."

But I think what I'm taking away today overall is that everything that's been discussed today is not an afterthought, is not good to have; that if we really want to do high-quality research, everything that's been discussed today must be incorporated.

It's not a "like to" or "wish to." It has to be a "need to." So that's the major thing I'm

taking away today.

MS. EPPS: Thank you. Thank you for that. So on that -- thank you. Oh, go ahead, please. Thank you. Thank you, Ms. Burgess.

MR. BURGESS: So I don't really have, like, a big takeaway from today, but I do want to highlight something about in clinical trials, that the doctors should include the patients in the big discussion about what's going on, and they should include the patient's opinion no matter how they are, because although the parents have a lot more wisdom and they're a lot older, I feel like it's the patient's life that's being affected mostly, so the patient should be having a big say in it.

And yeah, that's it.

MS. BURGESS: Michael, you didn't have to say, "A lot older," but that's okay.

MS. EPPS: Thank you, Michael. We needed to hear that, specifically.

So anybody can answer this. How can collaboration between community, industry, and

academia, and FDA regulatory agencies improve inclusivity, including people in pediatric drug trials? That's a lot. Sorry.

Please.

MS. WILLIAMS: I would say through an integrated approach within underrepresented communities, combining medical treatment with comprehensive family and community support to create a robust network that helps families navigate this complex, fragmented system and the challenges.

I believe this approach ensures that the emotional, social, and practical needs are met, promoting resilience and better overall outcomes.

From a regulatory standpoint, it should be strongly considered incorporating clinical trials into the conversation as a standard with the mandated checkbox that prompt providers during the history and physical to have that conversation with families as another option to care as part of the comprehensive care plan.

MS. EPPS: Any academic partners want

to talk? Please, Ms. Burgess; go ahead.

MS. BURGESS: I think what we're doing now and continuing what we're doing is the most impactful. I think that word of mouth is more powerful than we think.

You know, I have a few of you -- I got your numbers; I got your information; I'll be following up with you, but just that few can touch more people, which can grow and expand.

This is a grassroot ground movement. And if we all are all on board, once I get home, I'll take it back to my tribe; right? And my tribe will then discover, okay; maybe this isn't as scary.

It's really all about word of mouth and being consistent and having all of the elements, the FDA, the researchers; we have the sponsors; everyone is coming together, creating a huge think tank.

But if we continue this platform, we can see this groundswell go even further. So I think it's just the consistency with this.

MS. EPPS: Thank you Ms. Burgess.

MS. LEWIS: Tamorah Lewis, a physician scientist from Toronto. So the question about collaboration is a really important one, and I've been having conversations with the IRBs -- and in Canada, we call them "REBs", about what role the ethics boards can play in diversity and equity.

And I think that one very -- what feels like low hanging fruit, is for patients and sponsors and regulators to all get together and talk about, you know, what would maybe a universal budget template look like.

If we were to design a trial with the most marginalized and the most disadvantaged families in mind, what would be all the key budget items that a sponsor or a site would need to consider in order to allow for true unburdened participation?

Because right now, I feel like every IRB is struggling with this and reinventing the wheel. Each sponsor is kind of probably doing some version of this, but it doesn't have to be that way.

We could collaborate together and come

up with some template that could be universally used, and with the key input of the patients and parents, not miss any of the important details that even we probably don't understand

MS. EPPS: So universally used and user friendly. Thank you. Thank you for that.

Anybody else want to tackle that question? Thank you.

UNIDENTIFIED SPEAKER 8: Yeah, so one more thought. So as we think about how to our obligation to patients, we want to ensure that the clinical trials that we enroll them to are high quality and likely to generate impactful, meaningful results.

And so along those lines, I'd like to go back to some of the data that Pam presented this morning around multiple trials enrolling for specific conditions with small populations.

So it's interesting to think about is there an opportunity for academic centers, along with regulators and sponsors, to coordinate efforts around

diseases or specific drug types, such that we can prioritize a limited number of high-quality trials that are most likely to generate the results needed for that population around a specific therapeutic, as opposed to maybe the current model, where it largely sponsors who are responding to requirements and are sort of forced to conduct multiple trials in parallel for a given condition, but they're drawing from such a small population.

MS. EPPS: Thank you very much. Other thoughts on collaboration? I'm going to put you "youngins" on the spot, because, you know, Michael, you said we are a lot older, and, yes, I am.

But what do you all have is wisdom? And I really would like to hear from the patient represents again about collaboration, any thoughts you have.

MS. SARI: Sorry. We're sharing, yes. So on collaboration between these institutions, I think that it's really important that from, I guess, a regulatory side that certain standards on diversity

are set up, but they're set up in such a way that, because it was said before in a question from virtual attendees -- they were wondering if these diversity requirements might impede the process of a trial or slow it down.

And I think that these groups need to collaborate, and they need to find a way where they can have effective and excellent clinical trials that are also diverse.

And I think from a regulatory side and from an academia side and from an industry side, that level of collaboration really has to happen on that specific issue.

MS. EPPS: Thank you. Let me ask a slightly different angle of the same question on follow-up -- what you said Nasrin about having regulations. That's where people are being told they must do these things, but there's another -- so that's a mandate in regulations. There's also incentives in regulations.

Are there areas of incentives that you

think that might make people, you know, want to be involved in some of these activities?

And I'm not asking just you or that is a question we answer right this second, but if someone has some thoughts on that right now, that would be interesting.

MS. SARI: Are you saying incentives for patients or incentives for these organizations to be more diverse?

MS. EPPS: For those who are involved in these activities. So yes, definitely organizations.

I can tell you right now, there are incentives for, you know, sponsors who are doing drug trials to do them. We have certain incentives. You know, what they say or how they set up, you know, those exist. If there was some idea of an incentive of what you think might have people be more involved, I was just curious.

MS. OGUNO: I can try to answer just quickly. I'll be taking a step back to your previous

question in speaking about the collaboration between patients, healthcare, academic and industry, and the FDA.

I think listening to what really matters; my experience in sickle cell and other aspects is looking at the endpoints; right? One of the critical aspects is that we're looking at, oh, for example, pain.

This is what clinical endpoint is that's critical here. This is what we're looking at; this is what we're testing. Where the patients might say, "I don't care about pain; it's the fatigue."

That's what we need to solve for. So while everyone's focusing on one area, maybe listening to the participants. So what really matters to them helps us to develop better clinical trials, develop better molecule that addresses that, and then work with the FDA or other organizations to look at endpoints that addresses what the patients are actually looking for versus what historically we had looked at as data, which might not even be meaningful

as we develop drugs.

So I think that's a way we can triangulate, in terms of what really matters. We know what's historical, but what's critical now, and how do we as an industry, as caregivers, as the patients, and as regulators develop what's critical in how we look at this indication or this treatment or this disease, and move forward.

MS. BURGESS: And to add to that, I feel, speaking as a parent and a mom, as an advocate, I'm a professional advocate for a living for my nine to five.

I think it's really important to advocate for lifting the barrier, the weight of clinical trials from the families, the financial weight; having an incentive for even something as simple as gas -- you know, just travel; having an incentive, you know, something as simple as a grocery store gift card.

And I say that with the fullest of transparency, because having a child with a chronic

illness myself, I jokingly call it "hospital living," where we're, like, living in the hospital sometimes weeks at a time.

And then to participate in a clinical trial on top of just getting out of the hospital, sometimes finances -- you are drained. So having an incentive -- I heard someone say, "Lifting that barrier, that" -- excuse me, "that burden from the families would be so helpful from a family/patient perspective."

MS. SIMPKINS: Yeah. You know, Tamorah brought this up, about the bioethics and thinking about this from the IRB perspective too.

When I think about this from the topic of collaboration, the reasonable reimbursement for time, burden, and effort is something that there seems to be some confusion, even though I don't think there really is that much confusion; right?

And maybe some IRBs look at this differently, although there have been a number of webinars saying, "Hey, Industry, you kind of have

gotten this wrong; the IRBs are allowing this."

I think the bigger conversation and when we talk about this space of collaboration, this is something that should be very clear so that everybody going into it actually knows it's a matter of equity and that they're not doing the wrong thing; they're doing the right thing.

And I do believe that message through the collaboration that you were talking about can get out there much more quickly so that -- it's not ambiguous; it's not, but for some reason there's still the perception that it is,

MS. EPPS: Let me ask you all a related question along collaboration and lack of ambiguity and so forth, and it's the issue that's been talked about several times, which is transparency.

So what do we do in a sort of collaborative space to improve transparency, so we really can assist families in making decisions about being part of this process? What are your all's thoughts on that?

Dr. Yao is busting at the seam over here.

Please, go ahead.

MS. YAO: I don't know if this is too controversial for -- what, 4:15 in the afternoon, but, you know, I've been thinking a lot about this, and one of the things that -- I guess Tamorah sort of brought it up on this panel, but, you know, we don't know how much things cost.

And one thing that it would be helpful to know about and be more transparent about is how much does it cost to do this? Because I think it would be really helpful in understanding where that money ought to go if we know where the money is currently going.

And that's one place that -- and I'm not sure that it would be appropriate for FDA to be involved in that conversation, but I think it needs to be a part of the conversation, because it all comes down to -- everything I've heard about all comes down to, well, you know, this is going to cost some money.

And so how do we create the efficiencies? How do we create the right place for the money to go, you know, for getting these trials to incorporate all the things we've talked about today?

How do we know how to do that if we don't know how much things cost? So I'm just going to throw that out there.

MS. OGUNO: I think there's also the opportunity, when you're having a discussion with your participants, to understand what are the challenges and take that back to the sponsor.

So being me, on the sponsor side, I'm knee deep with my team in developing the ICF, developing the budget for the sites, and I am emphatic about whatever the sites need -- transportation, reimbursement, let's make sure we have it in the budget, and they know that, so they can also pass that on to the participants.

So I would, on the other side, raise your hand and say, "Hey, can you approach the sponsor to reimburse for A, B, C?" Because, to your point,

sometimes we don't know what we don't know. We don't know what the patient experience really is from one that's in California to one that's in New York -- one that's at Texas. It's very different.

So I would encourage you to take that back to the coordinator, to the PI, and say, "Is there an opportunity to have this reimbursed, because this is a burden for us."

And maybe you didn't think about that when the study was being designed or the ICF was being developed, but it is, and I -- at least for me, but I'm sure with my colleagues as well, they will absolutely take that back.

And whatever is to make it right, we will do; we just need to know about it.

MS. RANDELL: When I think about transparency, my mind goes to having really vulnerable conversations with families during clinical trial discussion and recruitment.

So, you know, I think helping local research teams get really comfortable feeling

uncomfortable and being willing to open space to discuss hard things will allow racialized and marginalized communities to engage with research in a way that they haven't been able to before.

So, you know, being able to ask about, "What's your family's experience with your child's medical care, and do you have any concerns that there might be different experiences based on your family's identity?"

You know, "Do you have any fears or concerns about participating in research, based on your culture or based on your family's, you know, cultural history?"

You know, those are very simple, basic questions that we don't ask that could create a safe space for families to discuss things that could help them overcome their mistrust or, you know, their fears. But we don't create space for families to discuss those things when we talk about clinical trials. And that's not transparent.

Like the way that we do it right now,

it centers our own comfort. And so, you know, I think that there's so much space for creating curriculum around this, creating education around this so that research teams can become more comfortable having those conversations.

MS. EPPS: I'm going to bring up another thing that maybe at 4:15, 4:20 we shouldn't talk about, but money makes people uncomfortable. But it goes along the lines of what you're talking about, difficult conversations.

And they certainly run all across healthcare. Like, people -- you know, I have elderly parents talk about things, like advanced directives. Nobody wants to talk about that with, you know, somebody who is 90 something years old, and yet they should.

But to get to my point is -- let me first just ask, have any of you all had a bad experience within a healthcare system? So not necessarily a provider, but another part where someone didn't treat you right? I know I have.

And for me, it's the accountability when people are -- you know, do you feel comfortable, you know, telling somebody, "Those folks over there just didn't treat me right, and this is why I think so; this is what they did, and this is why think so." And, you know, having systems for accountability for that, because it exists. I know in my experience.

I don't know if you all wanted to speak to that -- any of you all.

MS. WILLIAMS: I can speak to that.

MS. BURGESS: Yes, I --

MS. WILLIAMS: Okay. I can speak to that. I get doctors, nurses, they're overworked. They have far too many patients. And there was a time where I was mistreated, and I learned the power of the Department of Patient Relations, and I expressed my grievance to that, and it was addressed quickly. But, you know, just having empathy for the doctors and the nurses is important.

But I just wanted to go back to the previous question about transparency. I feel -- I

don't know what the right answer is, but I feel like there needs to be some sort of quality improvement built into this in the sense of capacity-building projects.

How are these dollars being spent by these systems? Because from what I observed in my previous work, working with federally qualified health centers, I was trained as a quality improvement coach to go in there and find out what their gaps are.

And we did things, like process mapping and PDSAs. And a lot of it, when you get to the money part, they were not allocating those resources properly.

So when we went through the process and we redesigned their workflow, you know, we were starting to see an improvement with their patient screening rates and vaccination rates with youth.

So I don't know if that's the same concept that can be used in a clinical trial process, but maybe it should be considered we, because systems are not going to be forthcoming and say, "Hey, I don't

know how to do this."

But if we have a team to work with them to improve their process, perhaps that could be how resources and sponsors can spend their money with the capacity building project.

MS. BURGESS: Thank you for that comment.

As a parent, I have experienced great discomfort on numerous occasions on how I was treated in the ER once I brought Michael to the hospital when the pain crisis had escalated to the point nothing would work at home.

So the validity of suffering was something that, unfortunately, was not validated, even by the healthcare professionals. And I remember specifically a nurse letting Michael sit for hours screaming and crying and suffering.

And so with that being said, you know, going back to what we originally were talking about, I just think that using the voice is powerful.

I spoke to patient relations right

away. I let them know what was going on with my son, and it escalated all the way to the top at the hospital. And that nurse actually has never worked with Michael again, and he was 13 at the time.

So I think using the voice is powerful, but when it comes to clinical trials and doctors becoming very comfortable in the uncomfortable and engaging and clinicians engaging with families about uncomfortable conversations, you know, families, like myself, we will open up, and we will talk, but we have to feel like the playing ground is level.

So patients will open up. We'll say what we need. We'll make sure that the voice is heard, but if -- I think the comment was made earlier, "But if we feel talked at, instead of talked to, then we'll hide."

And that's when you won't have the participation. That's when families will, you know, pull back, instead of families being retained to go the long haul in a clinical trial.

So, you know, it's all about patient

voice. It's all about collaboration. It's all about feeling like we're heard and we're seen and just keeping that accountability going between the relationship, because we're all at the table at this point.

MS. EPPS: Thank you very much. Let me ask you then a question. There's a question from online, and it ties somewhat into what we've been talking about, about collaboration and who you trust.

And it starts as a comment, that "There seems to be an evolving trend in the pharmaceutical industry to move away from pediatric centers of excellence or pediatric groups within the companies.

What actions can be taken to ensure pediatric needs, with kids who are an underserved group, receive appropriate attention and priority within pharmaceutical companies?"

So I guess my question is a little bit broader than that, which is just sort of the idea of especially if we're trying to get out into communities, there are not Pediatric Centers of

Excellence all over the country; right?

So what do we do to get the level of excellence we want, given that may or may not be attached to a so-called "Center of Excellence" in the pediatric are?

Or should we just make sure there's some sort of connection at all times that way? Is that feasible?

See, I made the harder questions for the end of the day; right?

Or let me rephrase this. Have people received care within primarily pediatric-focused centers are your experiences, or do you have experiences where the care is largely outside of a pediatric center?

MS. SARI: I mean, in what I've experienced, it's been within pediatric spaces. And, I mean, I can't speak to what other people are experiencing, and I don't know if that is a trend that person was commenting on, but I haven't personally experienced that.

MS. EPPS: Anyone else? Okay. thank you. Yeah, I mean, I wish Dr. Kipp were still here, because I know --

UNIDENTIFIED SPEAKER 9: Yeah. Maybe -- yeah, I can --

MS. EPPS: -- that she works with the communities that don't have large centers of anything near where they live. So she may have had somewhere to say that yes, please,

MS. HILDEBRAND: Yeah. Heidrun Hildebrand from Bayer. If I understood that question correctly, I think it was looking more inside of companies.

And I think what may confuse patients, clinical site, academic centers at large is that we in industry are used that we somehow get reorganized every month -- no, but every two years at least, and with that reorganization, names of department and groups are changes.

So there might be that the word "pediatric" get lost in the new name, but that doesn't

mean that the expertise, which is available in the company, has vanished.

It may be grouped differently also. And I can very much understand that for people from the outside or for patients and also for sites who used to work with the person with a certain name tag, and now the name tag changed, they think maybe the focus has changed.

But I would think that is really due to the mania in industry to reorganize every time and ongoingly.

Thank you.

MS. EPPS: Thank you so much.

You know, we've been talking also about sort of things to do to build that take investments, whether, you know, it's finding funds or finding -- putting groups together.

Let me ask you something sort of to maybe there's some low-hanging fruit that people could focus on now.

So let me just ask you, are there

specific activities or features of a clinical trial program that would make you feel the trial is inclusive, that are things that maybe, you know, could happen sooner and later, such as transportation services or offering the materials that are in large print or in a certain language?

So is there any specific activities you say, "Well, look, that should be achievable -- doable, you know, sooner, rather than later," that again makes people feel included -- makes them feel inclusive?

Go ahead.

MS. YAO: I'm not going to speak for the people who are on the front lines designing the trials and the patients who, you know, obviously want to provide.

It's critical -- we've already heard, that we get patients to provide their input from the beginning to hear what those barriers are, what the burdens are.

But as I'm thinking about it -- and I think Martha Donoghue was asked kind of the question

about, you know, is ADEPT going to be required in a pediatric -- you know, a PIP or a PSP? How is ADEPT going to be implemented by regulators?

And regardless of the process we do or we use to incorporate the things that we've heard today, whether it's a DAP or in the PSP or in the PIP -- I think what I've heard today and when I think low-hanging fruit, from my perspective at FDA, is when we send comments back to a sponsor about, you know, "How have you considered increasing the diversity of your clinical trial in children," we can give them concrete questions that we can ask.

"How are you decreasing burden? How are you allowing for patients to -- how have you incorporated the patient's voice in the design of this trial?" I mean, we can ask those questions directly as we work with companies to help incorporate some of the suggestions we've heard today.

So I think that's one way that we can easily -- FDA -- I say, "easily" -- nothing is ever easy at FDA, but easily, I think we could begin to

implement even just asking those questions as part of pediatric development plans.

MS. EPPS: So I'm just going to quickly say I speak FDAE. So I'm just going to translate a couple of things. We love acronyms. DAP, Diversity Action Plan, it took me a minute to remember that. And PIP is a Paediatric Investigation Plan.

So these are things that they're related, but just so people are tracking. So yes, thank you.

MS. SIMPKINS: So from the industry perspective, and it builds on what you're saying, it's actually -- it's circular; right? How do we do it? And then you also make sure that we're accountable for it, because if we're not doing it, you're going to ask about it.

But some particular sort of low-hanging fruit that I can think of in this space are both about the process and then a couple of examples about specific activities.

So obviously everybody talks about

trust. You need to have the trust in place, but the co-creation from the beginning, you can co-create an inclusive trial, and who are you bringing in to have these discussions, and how do you have that continual discussion.

So we've done this in the adult space in kidney, and having a standing counsel that is actually looking at diversity in a particular trial.

And so there's another topic of we can have that council in place to have the trial, like, as early on -- you know, all the aspect of study design and study conduct, informed consent, all of that.

But then when you have this group in place, you can go back to them with transparent information and say, "Okay. This is where we're at with recruitment and retention." And actually say, "All right. Percentages here are this."

And that's been incredibly useful, and it really builds trust, where you're just very open and saying, "I don't understand," or, "This is what's happening," and, "This site is not really recruiting."

So having that ongoing conversation.

And then within that group, potentially, we've had a really good experience bringing patients to PI meetings and talking about the topic of diversity.

And so we've done it sort of at all stages, and now, one new trial, we're going to do it at the very first meeting.

And I think that hearing it from the patient and patient community and from a sponsor bringing that, I just think it sort of helps that whole credibility and transparency.

Another step there that has been really useful I think is -- and people have talked about this, who are the credible messengers, and how do you get the information out?

So when you're thinking about an inclusive trial and you have co-created materials, well, there are a number of patient groups that have ambassadors that can provide that peer education, and that sort of immediately brings the credible

messengers there and raises awareness about the trial, so it's the dissemination piece as well.

But then in specific activities and, I would say, low-hanging fruit, it is really important though. So maybe it's not as low-hanging, because we don't always think about this.

But specific activities that are related to disability can very quickly help with inclusion. And I feel like this is not something that we call out a lot.

And the disability could be specific to the condition, or it just could be because people have disabilities, and how are we making our trials inclusive?

And I think that if we think about this, it's going to be -- there's always a tagline in this space, essential for some, helpful for all.

When we think about the sites that we're selecting, I think physical accessibility is something that we need to be thinking about.

But when we're thinking about the

creation of materials, there's very low-hanging fruit that can be done to make materials accessible; right? Do 16-point font. Don't do lower than 16-point font. Have everything closed-captioned and a number of other very tangible examples in this space.

And then even when I think about DCT, which could make a huge difference for people with disabilities, if you're not intentional from the beginning and creating your digital accessibility, then you're actually still going to be excluding a large group that doesn't need to be excluded.

And so I think it's low-hanging fruit, but I just don't think we talk about it enough.

MS. EPPS: Thank you. I have a follow-on question about that -- follow-on, sort of segue question.

And if I may, Michael, I wanted to start with you. If I recall, you're on an advisory board; is that correct?

So I mean, where are you involved in activities? You know, are they asking about stuff,

saying, "Hey, we're planning to do something, like, next year," this and that? Do they ask you thoughts there, or what sort of ways are they asking you to help out?

MR. BURGESS: So one way that -- an activity that I have helped with planning is a prom that they have every year for the hospital patients. I think it can be any teenagers.

But yeah, I help. Me and the other kids help plan the prom and, like, what floor it's going to be on and what's going to be there, what type of music, and how long it's going to be, stuff like that.

MS. EPPS: That's great. And so the prom, was it -- who had the idea of the prom? Why did they want to do it? Did they have kids feel like the hospital was someplace that wasn't just a place where you got stuff done to you; you could also have fun, or what was the theme to do prom?

MR. BURGESS: So I don't know who first came up with it, because it's been out for a while.

But yeah, the main idea was just to have the kids have fun, even though they're in a hospital; they're missing their own real dances at the school.

MS. EPPS: Got you.

MR. BURGESS: They can still feel like they're included and still feel like they don't miss out on these important events in their life

MS. EPPS: So they can have a little bit of normal life even when they're not in their normal life space, like home?

MR. BURGESS: Mm-hmm.

MS. EPPS: Yeah, that's really interesting. Thank you.

Well, that sounds like important low-hanging fruit. No. I mean, kids want to feel like life is normal -- right, whether they're in a trial or not. And so if you can do activities like that to help a kid, that sounds a worthy to me.

So let me ask then, how do we create -- again, this is my not elegantly worded, how do we create space for you all, Michael, Nasrin, Anvita, and

kids and their families to take an active role in designing and being involved in how these trials are designed and conducted? What are things that you all think needs to happen from anyone?

MS. SARI: In terms of creating space, I think it's really important to create channels of communication. I think sort of it's been touched on, the way that we disseminate information to communities, but then also the way that communities can express their needs, and not just communities, but also individuals, can express their needs as patients or as parents, because in the pediatric space, family is also really vital.

And so I think just in terms of creating space, you have to start with communication. You have to start with creating channels for communication between, you know, research institutions, between primary care physicians, between patients and their families, and, you know, not just one line of communication, but several -- interlinking these groups to build the most effective solutions to

issues presented by patients and their families or to needs or constraints from researchers or organizations.

MS. OGUNO: One thing that I can add that I think has been really helpful for us at GBT and, you know, afterwards is implementing patient advisory boards to review your protocol, not after implementation and it's not recruiting, but a year before.

We have an idea of when the protocol is being developed -- submitted to the FDA. Bring a patient advisory board together. You don't have to have the full protocol developed. Schedule of assessment, inclusion, exclusion, how does this impact you? Would you enroll in this clinical study?

And we also have the opportunity to select where the advisory board is -- where they're coming from, so making sure that it's geographically diverse, racially diverse, all the different diverse aspects that we want to make sure we get feedback on.

So I think this is a call to the

industry to involve patients in the very beginning, not when things start going south, because we're not recruiting.

And it does provide benefit. There's such insight that you're able to glean and take the data back -- right, to say, "Hey, CEO, I know you're not going to like this, but we need to include A, B, C in the protocol, because the response is this is not going to recruit. We need to include A, B, C site or A, B, C country to make sure that it's diverse enough."

So it's an opportunity that we can take back as well to get the feedback ahead of time, not just as a reaction.

MS. EPPS: So let me throw in real quick a little add on to the same question that's coming from online, because they're saying when you all are doing that, should the focus be on social determinants of health or racial and ethnic diversity?

And is it an "either/or" or --

MS. SARI: I don't think it is an

"either/or."

MS. EPPS: Yeah.

MS. SARI: I think that racial and ethnic diversity goes right hand in hand with social determinants of health. It's easily observable to see that they interact with one another and affect one another.

And so I think what you'll see is if racial and ethnic diversity is considered in the design of a pediatric clinical trial and that space is created, whether it be through, you know, cultural competency or anything like that, then you'll also start to see that correlates with impacts on social determinants of health. So yeah.

MS. EPPS: I kind of agree. No. So I'm hearing -- so you're saying get on it early -- right, when people get on it early, as far as hearing what the members of the community and families are saying about what the proposal is.

And great. Other things to do along that line?

MS. WILLIAMS: If I heard this correctly earlier that most trials are not looking at the diversity until the pivotal moment. And if that is the case, then we have a bloated pipeline.

So I agree with my fellow panelists that we must involve our community leaders, the stakeholders; they are the gatekeepers. And what I mean by "involving" them is to let them be a part of the design of a clinical trial for adults and pediatric patients, because they have the ability to raise awareness in their communities and mobilize their communities so that way you're kind of tilling the soil.

When researchers come in and they need to do this recruitment, you can go to your churches, your community-based organizations and recruit from within these stakeholder networks.

So I think it's important to look at it way before you get to that pivotal moment.

MS. EPPS: So let me ask you a really loaded question then. It's like in the U.N. where

they had the voting members and non-voting members.

When we're talking about who's helping to -- I'm going to blow this way up; right? No. But seriously, maybe not a 3-year-old; right? But how much of a boat do kids and/or their families, versus other people putting protocols together, have in what's thumbs up and what's thumbs down?

And I don't know it's a one size fits all, but is there a space? Is there a spectrum across, which there may be, in certain cases, a lot a weight given to the non-research part of it -- community/family part, on making some decisions versus others.

So I just wanted to hear people's thoughts on that.

MS. WILLIAMS: We need to continue to keep amplifying these young voices. You hear these young people today.

MS. EPPS: I heard them.

MS. WILLIAMS: It sounds like they've already got their medical degree. So amplifying their

voices to evoke that emotion is so important and critical, and they too can be gatekeepers to the community. They have formed their own groups.

So I think they should very well be a part of the conversation when decisions are being made about their care.

MS. SIMPKINS: So I actually think they have a tremendous vote. It is almost impossible not to consider when you hear it. So what I found really helpful is, from the industry perspective, to invite the budget holders, the decision makers in on these conversations.

And then, like, when I have -- I have several different standing patient councils, and I love to invite our clinical development team, because they're also going to be the ones interacting with the sites.

But I think it is -- how much of a vote? I think it's tremendously impactful, should only continue to be impactful. I actually appreciate the FDA guidance calling out sustained community

engagement. I think it is -- my perspective is it's a big vote.

It's hard to ignore. It doesn't mean that everything gets accepted and it may mean that that's where the transparency comes in of, "Hey, this is why we do it like this."

And it's the feedback mechanism of when a group makes a suggestion, and if it's a suggestion that you bring back and it's not taken, why it's not, because I think that builds trust too; right?

Just to understand the research process more. But I think it is, I think it's a big vote.

MS. YAO: As you were speaking, it made me think of the comment that Dr. Kipp made in an earlier session, that if you are coming in and deciding to agree to enroll in a clinical trial, this is very late; right?

And that there may be even members of your own community who question why you're doing it and that may even isolate you from the community, because you decided you wanted to enroll that trial.

But it seems to me if you turn it on its head and that you have those patients -- those trusted emissaries that sit at the table as a patient advocacy group at the inception of the development of that trial, that when the trial then -- it's time to enroll, that the person who was sitting at the table can say, "This was something we, our community, had a voice in, and I am there to prove it."

So it seems like that could kind of turn it on its head.

MS. EPPS: You know, we're coming near the end the time, and so what I'd like to do in closing this session out is to ask each one of you all to share, if you will, what your call to action would be coming out of this meeting. I'll start with my own. Just, like, kids and families speak up.

Anybody else who wants to share?

UNIDENTIFIED SPEAKER 10: I thought it was really interesting to see data around the willingness to participate. I think that an ongoing sort of misperception is that families from different

race ethnicities a less willing to participate.

It doesn't look like that bears out. And so really there needs to be more effort around how do we reach all these families. And so that's something that I'd like to think about.

MS. EPPS: Mine is on. You can walk up to whoever has got an open mic. That's strange.

MS. SARI: I guess the call to action, I would say that -- mentioned earlier about that gap between -- pediatric -- inclusive and diverse and how much wider is that gap for -- sorry, for people with diverse perspectives.

And I think looking into that and understanding that whether you are a patient or a community member or love someone who has a chronic illness or, you know, are working in the field, that understanding just how wide that gap is, is really vital in taking the first steps in moving forward to close it. So --

MS. EDWARDS: I think my call to action is that I see the onus on the industry and on policy.

You know, if it's not mandated, if it's not a requirement, if, you know, it's left up to our own intrinsic motivations, it's not going to happen.

So I think there needs to be some order. There needs to meet some requirements put in place, and then move from there. And I think that will have a trickle-down effect, because there is only one; they have no choice.

So I think some people are going to have to get in line to make things happen.

MS. UMARETIYA: I think for me, what Sue said earlier about thinking about the ratio of burden to benefit, rather than just risk and benefit, is something that I'll take away as a pediatric oncologist and someone that thinks about oncology clinical trials, because I think that there are a lot of things that were shared today that we could likely incorporate in our trial design to decrease the burden of participation.

MS. BURGESS: My personal call to action is -- I am on the iCAN volunteer board, as I do

the community engagement work of iCAN.

So my call to action is to create a community within the community that can really get around and embrace, not only, you know, getting clinical trials disseminated properly, but also coming together to feel that this community feels seen and heard, validated, and supported; that the community within the community feels, like, there's a cohesiveness there.

So if it starts there, then we can work our way out. So my call to action is to create this space within iCAN coming up in the '24, '25 year.

MS. SIMPKINS: So my call to action is, is at this table. I think involving adolescents and young adults is so essential, but also the innovation -- the different way of looking at it and the passion that you bring, so it's tremendous.

So I feel very privileged to have heard this, and this is my call to action, to continue to, and more strongly, involve adolescents and young adults in the co-creation process.

MS. OGUNO: Thanks. My call to action are, I think, two things, continue to listen early and listen often and getting feedback where needed and as appropriate with the indication that we're working in and then not being afraid to lean in into those difficult discussions, specifically with our sites and with our partners, in terms of how do you plan to recruit appropriately.

It's not something you want to lead it, but it's important now. So I think have some energy around that, and it needs to happen. It's not "should," "could," "would"; it must.

So having that intention to have those discussions early with our partners to ensure that when we're thinking, we're thinking with the end in mind, and it's not just, again, a response, but it's really what we intentionally developed.

MS. WILLIAMS: My call to action is to continue doing exactly what I'm doing and that's forging these deep human connections between underserved communities and medical innovators and

expanding my clinical trial program across the country, building up the stakeholders network so we can reach more people.

MS. LEWIS: My call to action is actually directed at the FDA. So I learned such inspiring things today about -- I think it's OMHHE, and this office and all the pilot projects that they're doing and all the things that they're investing in and all the things that they're learning.

But I didn't know a lot about that, even though I'm in this space. And so my call to action is for the FDA to really think creatively about how to share all these learnings across all these stakeholder groups so that we can all benefit from the amazing work that's being done in that office.

UNIDENTIFIED SPEAKER 11: Yeah, I couldn't agree with you more, Tamorah. I think that my call to action is, number one, to disseminate this information across FDA and to help to disseminate it across industry when we can.

I think the other call to action for me

is to co-opt Bella's phrase. And so in your sponsors now, when you go back and you see comments on your documents that when you've, you know, provided a rationale for why you can or can't do this, I'm going to start saying, "Yes, and."

So if you see that on an FDA response, you know where that came from. That came from this meeting right here.

No, seriously, I think that what I have learned today, I am still processing, but I think what we can do at FDA immediately is to put this information together, get it out in the public, and promote some of the programs that we already have at FDA to further the causes here today.

MS. EPPS: Thank you so much, you all. So if I heard it right, to sum up, you know, just what we already knew as kids -- what we learn in kindergarten, sharing. So if we share everything, we can really go further.

On that note, it's been my pleasure and honor to be moderator and to hear all you all,

especially you all young people who just amaze me. And so thank you so much. And on that note, I'll turn it over to Dr. Yao.

MS. YAO: So Michael and Nasrin and Anvita don't go too far.

Okay. So I have the enviable position of providing some closing remarks.

And, you know, one of the things I will say before I give you my key takeaways is that a lot of times at five o'clock, I'm like, "Can we just be over already?" But I have to say that the sessions today and the people that have been involved, particularly the young people, have given me kind of some energy.

So I'm kind of disappointed that we have to end now. But we do have to end now. So I'm going to give you just a couple of reflections on what my takeaways are.

And please, don't view this as the official FDA takeaways. These are just my takeaways. Some thoughts that I think were triggered in the

discussions today.

In Session 1, you know, what I heard was that FDA is doing some things, and we've done some -- we had that big meeting for adults.

Many of the themes, the challenges, the solutions, they're not that different in terms of what we have heard are the challenges in adults.

But there are unique challenges related to diversity in pediatric clinical trials. I think it's more challenging to provide equity in voices when those voices come from children.

I think that solutions for diversity in the pediatric space can't necessarily be extrapolated from adults, but probably there are some places where we can extrapolate.

I think it's going to -- you know, we've already done quite a bit to improve diversity, but I think what I've heard today is that we're just touching the tip of the iceberg.

And this notion of bidirectional communication, meaningful engagement, building trust,

and avoiding mistakes that may take a generation to correct were I think some poor key takeaways from the first session.

In Session 2, I thought we heard some excellent examples of inclusive trial designs. I was really impressed. It really impressed upon me that proportionate representation is just more than a similar population compared to the proportion with the disease.

You know, we need to think about what the real goal is. What is really good? We're not necessarily measuring what we ought to measure if we're just limited to race, ethnicity, age, and sex.

And we have to think hard about what the correct metrics are in order to, I guess, get it right or advance the real goal.

I heard a lot about being intentional and planning early, about what a representative population really means. And that doesn't necessarily mean it's those four areas.

It might mean the disease

considerations. It might mean the geographic considerations. It might mean who has the burden?

Inclusive trial designs, I heard this a lot, and I think this is a clear takeaway that patient-centric trials don't just mean that we invite someone to come in at an advisory committee and chat about a trial that's already done. I think it means, you know, throughout the lifecycle of drug development.

And I heard that decentralized clinical trials aren't cheap, but there may be ways to increase efficiency, and with that increasing efficiency, maybe it will ultimately be cost effective to be inclusive.

Panel 3 was just terrific, and I have too much here to really go over, but I really have to give credit to those who were a part of Panel 3, particularly our young panelists.

You know, we talked about what is community, how does community affect enrollment, community based engagement, and how do community institutions build and maintain trust. So much there.

So rich.

And I won't read through this, but hopefully we'll be able to share it with you as slides in follow-up.

Oops. Screen sharing has stopped. There you go. Screen sharing has stopped, and the shared window is closed. There we go. I don't know what that zoom thing is. There we go.

Session 4, you know, I think -- we heard a lot from Session 3, but so many great talks about recognizing structural racism; that it affects the ability to enroll children in clinical trials; that community engagement, but also clinician engagement is important to promote health equity.

Effective communication and comprehensive holistic care is again, an important way to encourage families and children to both enroll and stay in clinical trials.

And I think the talk from Puja was great about opportunities to advance clinical trial equity in pediatric oncology.

And, you know, one of the things that I heard was that, you know, the enrollment in clinical trials -- we saw this in a lot of data today, that enrollment in clinical trials didn't vary a lot by SES.

I think some of the data that Pam presented, it looked pretty good, but it doesn't tell the whole story. And I think that's what impressed upon me; that just looking at kind of the data on the diversity in the clinical trials doesn't tell the whole story.

Where are we going? What's going on here? Okay. This thing has a mind of its own; doesn't it? So I can't move it now.

Here we go. Session 3, Session 4. There we go. Session 4.

Anyway, just some thoughts. So before we end today -- and I did want, if I could, call up Michael, Anvita, and Nasrin to the podium, please.

So talk about brave; right? I mean, can you imagine coming up here, like, a, you know,

young adult or high school student to a bunch of professionals here?

I think if we could just give them really our thanks and appreciation.

And I also want to acknowledge -- thank you. Thanks to all three of you. Really terrific.

And I want to acknowledge Sneha too. But you know what? You're too old now.

Imagine that, Sneha, you're too old now. But thank to Sneha too for your participation.

And then finally, can we advance to the last slide? Maybe? Oops. There we go.

Before we end today and before I adjourn, I want to really thank all the presenters and panelists. Fabulous job today from all of you. I can't tell you how much I learned. It's been really a wonderful day.

Thank you so much to our colleagues from M-CERSI, Dana, James, Heather, Eric, for the support.

And I need to have our folks here on

the side who ran the session today, Julie, Iana, and Reed, thank you so much for OND meaning support.

And finally to the staff that we have in the Division of Pediatrics and Maternal Health, particularly Carrie Ann [ph], Michelle, Meshaun, Carla, and Lily. I mean, you guys did a fantastic job in organizing this meeting today.

With that, I'd like to adjourn the meeting. Oh, sorry, one last thing. I meant to say this at one of the breaks, and I forgot.

Part of the beauty of being back in person is making these personal connections, so don't be shy. If you see someone wanting to run out, grab them and say, "Can I just get your email, so we can talk later?"

If you can, stay for a little bit after we adjourn so that folks can come in and talk to each other about what they can do and how you can help, I would love for that to be another outcome of the meeting.

Again, thank you so much for joining,

and thanks, again, for everything. Bye.

(Whereupon, the meeting concluded at 5:07 p.m.)

CERTIFICATE

I, RICHARD LIVENGOOD, the officer before whom the foregoing proceedings were taken, do hereby certify that any witness(es) in the foregoing proceedings, prior to testifying, were duly sworn; that the proceedings were recorded by me and thereafter reduced to typewriting by a qualified transcriptionist; that said digital audio recording of said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

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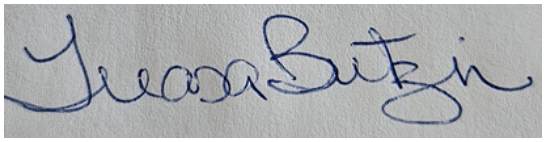

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