INCREASING PATIENT PARTICIPATION IN CLINICAL TRIALS

PANEL 3

Improving the Informed Consent Process

One of a series of live panels from the WCG Patient Advocacy Forum in Washington D.C. in October, 2019

As protocols grow more complex, how do we ensure truly informed consent? How can we ensure patients and caregivers understand what they are signing? How can the patient voice be incorporated to improve the process?

These discussions have been significantly edited for clarity and length.

The Panel

MODERATOR

Lindsay McNair

Chief Medical Officer
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PARTICIPANTS

Mary Elizabeth Williams

Journalist and Author

Kristina Wolfe

Eversana, Our Odyssey PAG, and Patient Advocate

Alyssa Lanzi

Speech-Language Pathologist and Clinical Researcher

The Forum

Lindsay McNair

Ok, so shall we start with everyone introducing themselves?

Mary Elizabeth Williams

I was a patient in the first cohort of a clinical trial for immunotherapy in 2012. I realized later when I was writing a book about it that I had not understood the consent process at all, and when I read my informed consent papers again, I realized how really confusing and obtuse they were. I hadn't in the moment, because I was traumatized and scared and sick. So now, that's kind of the thing I like to talk about.

Kristina Wolfe

I have a background in public health, health economics research. I also have a background in managing clinical trials. A lot of what drove me to get involved in all of this is my chronic disease, type 1 diabetes. I've done a lot of my own advocacy.

Alyssa Lanzi

I'm a clinical researcher at the University of Delaware. Primarily, I investigate treatment approaches for individuals with neurogenic communication disorders, most commonly dementia or mild cognitive impairment. I'm also a speech-language pathologist and educator of graduate students in my university.

Lindsay McNair

One of the things we always say on the IRB side is, informed consent is not the informed consent document. Informed consent is a process.

"...when I read my informed consent papers again, I realized how really confusing and obtuse they were. I hadn't in the moment, because I was traumatized and scared and sick."

—MARY ELIZABETH WILLIAMS

It's a conversation, and it's not just on the day of screening - it goes on throughout the duration of the study.

But there's so much focus on the informed consent paperwork and what that says, and whether you've run it through Flesch-Kincaid software in Word. That's silly, because all that does is look at the length of sentences, the number of words in a sentence and the number of letters in a word. You could actually write the whole consent form backwards and get the exact same Flesch-Kincaid score.

It says nothing about *understandability* of documents.

Many groups have been working on trying to improve informed consent and the informed consent process. A lot of them, of course, focus on the document, because it's what we can change when we're not there in the room for the conversation.

The Office of Human Research Protections, which is the regulatory body that oversees all federally funded research, in January put into their regulations a requirement for informed consent documents called the "key information section." At the beginning of each document, there needs to be a concise (which is not defined) statement about the most important things a potential research participant would want to know when they're considering whether they want to be part of a study.

There is no real guidance about how to actually apply the key information section criteria. So many institutions have come up with

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—LINDSAY MCNAIR

their own guidelines. Some say it should be less than a page, some less than three pages. We came up with a guideline of one-tenth the length of your consent form or three pages, whichever is shorter. It is a very subjective thing to say, "Pick what's most important to the people who may be research participants," because that's going be different to everybody. For some, the fact that you can't drive during the study may be important. For people who live in Manhattan and don't drive, that may be not important to them at all.

Because this does not replace the rest of the document's content, it will make the informed consent form longer. There is also some effort toward improving communications with something called the "Universal Patient Language." You can see it on the website, UPL.org. With many, many focus groups, they came up with a way to communicate information not just for clinical research participants, but also for patients for their marketed products.

UPL is intended to be used for all communication. If you go on their website, you'll see a sample informed consent document. But it's not just about language and translating medical terms into lay language. They also talk about format and layout and margins and font size and framing paragraphs and converting information into tables and figures and using diagrams rather than just writing everything out in long paragraphs. So we are starting to see a few companies working some of these concepts into informed consent documents, but we haven't seen widespread adoption yet.

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—LINDSAY MCNAIR

What do you think is one of the most important factors that goes into some of these decisions about whether individuals want to participate in a research study when they're offered that option?

Mary Elizabeth Williams

Well, for me, it was very easy because there are still very few treatments available for metastatic melanoma. But an important factor was feeling like I was in an environment of trust, feeling like the people who were talking to me had an investment in me and knew who I was, saw me as a human being. And any encounters I had in the medical process with people who didn't see me as a human being, informed my decision.

There was one person along the way who, if he had been the person who was my primary point of contact, I wouldn't have enrolled in that trial and nothing would have convinced me to. So the human interaction, there's so much that builds up to that moment. There's so much that goes on behind the curtain, and then the moment you're sitting face to face with someone, that's the moment of choice. Everything that's come before it might not matter if the person delivering the information isn't sensitive and respectful and empathetic to you, which is scary, but also there's so much power and there's so much potential in that.

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Kristina Wolfe

I agree with you; those are very important aspects when considering participating in a clinical trial. I think beyond that though is seeing us as full people, beyond just patients. For example, the scheduling aspect

has to be incorporated into that consideration as well. When there are too many procedures or too many site visits, or too much time on site, those must be brought into consideration. I think for me, as a young adult, the clinical trial I enrolled in I had to drop out of. I was in grad school. There were too many things to consider in going to those visits to the site, and I wanted to continue, I wanted to continue to be involved, but the protocol schedule didn't allow me to do that with my already busy lifestyle.

Alyssa Lanzi

I try to always teach our students and our research assistants the importance of communication and the importance of that personal interaction from the first encounter. That is much beyond this one-hour session that starts the informed consent process. But it's an interaction, a communication in a positive environment that starts the moment you schedule a session, or the moment you greet the individual. That's so critical.

Are they going to be comfortable enough with you in the session to ask you questions if they're unaware of the information in the informed consent? Will they feel confident that you're going to give them the adequate information? I stress importance of having that personal interaction, that conversation in the beginning.

Something I always like to start with is, "Tell me your expectations for today." Because for me a lot of times, it could be that their daughter forced them to come here, because they're starting to notice memory

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impairments, and that's a really different conversation than I would have with someone who is a retired professor and just interested in getting involved as much as possible in research. So really opening the floor to conversation from the beginning is critical.

Kristina Williams

I think it begins even before that. It's that warm introduction to the patient. In this day and age, most patients are being recruited online. If I'm filling out this pre-screener form, and I fill in all of this information about myself, I'm clearly seeking information. I'm seeking somebody to contact me within 24 to 48 hours. I want to know if I can be a part of this now. If a response time is delayed, that's going tick me off. By the time I get to the site I'm already going to have that bad perception.

It comes down to actually recognizing it is customer care and treating patients as consumers.

Lindsay McNair

Alyssa (Lanzi) has written an article about the importance of having caregivers involved in the process of getting feedback on study design, because of her role and work in the lab with dementia patients. Alyssa, can you say a few words about that article and your experience?

Alyssa Lanzi

When I was approached to write the article, it seemed so natural to me that caregivers would always be included. It seemed quite obvious. Then I quickly learned I'm a minority. So it has been a really interesting

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process just trying to figure out, how can I teach others to think naturally the way I do, about including caregivers?

A lot of times, it starts with our conversation on the phone or when we're recruiting participants: "Who else is with you? Would you like to bring somebody with you to the session?"

I think a lot of people may not know they have the option to bring somebody with them to an initial appointment. Having that conversation up front with them, telling them that other people have found it beneficial when they bring someone, is really important.

I think the other thing is then, thinking of the caregiver as an extension of the patient, and as having their own identity. I say that for two reasons. First, if you're doing a clinical trial that involves home practice, or is going to have questions, you need to make sure the people living with the person or often interacting with the person, are aware of the clinical trial they are involved in. That's really important—because, of course, they're an extension—to make sure they're managing their appointments or things like that.

But second, without a doubt, caregivers also have their own role. In a lot of the research studies we do, we make sure we have a separate section for the caregiver and involve them as a participant in the study, so they have their own informed consent. They are research participants, giving us more information about the patient and their burden and things like that. We have found that approach really successful. We often do the

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informed consent process for both the caregiver and the patient in the same room, which allows some successful conversations as well.

Lindsay McNair

When you went through the consent process, Mary, was there anybody in the room with you?

Mary Elizabeth Williams

I had two young children at the time who were in school. I had a spouse who was at work. So I was alone. I was seated in a room. I had a very nice nurse who went through it with me. Her assumption was that I was going to say yes at this point, because I read the materials. But there were so many questions I tried getting answered beforehand. So many times, I would call up with one question that had occurred to me, and it wasn't this great back and forth conversation. I would have a thought, and I would want to call someone and talk to someone there, while it was still in my mind. That was really hard.

I also have experienced both of my children doing research trials. The other thing that can happen is where the people involved in the study look at the caregiver and don't look at the patient at all—it happens a lot with children—where someone would say, "Well, she's going to do this and she's going to do that." And it's like, "She's right there in front of you. You can talk to her and not talk around her, and not talk above her."

And I've also had that happen to me as a patient, where someone would be talking to my husband, and I'd be over here like, "I still am a

human. I'm not a vegetable. You can say it to me." Having that ability to understand that the conversation may be different between caregiver and patient, but there has to be communication with both of them. And there has to be respect for both of them at every level, no matter what their age, whether it's a two-year old or a 90-year old.

Alyssa Lanzi

These points are all so critical. Think about the assent process, if that person is the participant—even if they are not officially the one signing the consent form—you have a responsibility to make sure they understand to the best of your ability. Talk to them and not around them, because—guess what?—they're going to notice that.

The most important assets we have with us at the end of the day are communication and that personal connection. And patients are going to notice. I can promise you. I work with some severely cognitively impaired individuals. They will notice if you are talking around them versus to them. Even if you are doing a set process, make sure, please, please, please, that you're really making sure you talk to them and not through them or around them.

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Audience Member

Coming from a biotech perspective, we get pitched by vendors, especially in the space of giving folks information. In terms of informed consent, they have some technologies like chatbots, etc. that use artificial intelligence to get this information. But one of the questions we get is, "But does it remove that human element?" No one thinks there'll

ever be a transition to 100% AI-based conversations. But how far do you think that could go? The vendors are very ambitious and I'm a little skeptical.

Kristina Wolfe

That's a good question. I think that is the way things are shifting. As long as there's a human component that partners with all of that, maybe the human component or the cycle and your study coordinator could follow up on the bot-chat answers later. If we're targeting young adults in these clinical trials for example, they want the answers now. The robots and the bot-answer things are good interim solutions while they wait for a person to call.

Mary Elizabeth Williams

I met a couple of months ago with a company that's doing this kind of AI and they are very smart, very strategic. They started their work with teenagers, and they started with people with mental health issues. So they had an audience that was going to be built-in to be curious and engaged. They had a lot of success. The thing they really focused on was telling the participants to think of this as practice. Use this as rehearsal. Use these tools as a way to inform yourself about the conversation you're going to be having when you are in the clinic.

You get answers, but framed as, "This is the kind of conversation you're going to probably want to have when you step into the hospital and when you're talking to your provider or your nurse." I think that's very important to inform patients. "This is a tool for you, not just to get

information, but to train yourself and advocate for yourself and be able to follow-up with your questions, be able to articulate them in a way that is clear and concise to your providers."

Lindsay McNair

Alyssa, How would it work in the patient population you work with?

Alyssa Lanzi

I deal with a different generation and I can tell you as a clinician, I have seen plenty of patients who want to talk to the doctor, always. It's not changing by any means - especially in many of the skilled nursing facilities. I know that for a fact.

But I think what's interesting is a lot of times this idea of what's sexy in the research world - you know, what looks animated versus we're not looking at personal connection as innovative anymore. And I think it's funny now that a lot of times I'll have people say to me "Like, wow, you actually talk to the people!" Like that's so new.

All these robots and all of this new technology is happening. And I think it's one thing if it's going to enhance the research or enhance that communication, but by no means is it ever going to replace the communication coming from an actual physician or study staff, for a lot of different reasons.

I think there is a lot of opportunity out there for an enhanced communication experience. However, I think we are jumping very

fast—and without the appropriate framework. I know the big idea right now is, how can we incorporate Alexa or things like it into the skilled nursing facilities, and that is not working - *at all.* There's a lot of reasons but, you know, it's this idea that looks great on commercials, you know with this older population. But is it actually realistic? And I think the first thing both of you talked about as patients is that conversation, that personal connection, that feeling safe and confident that your needs are met in the beginning and trying to figure out how can we capitalize on that as well.

Lindsay McNair

That's a good lead-in to our next question. Different populations participating in or targeted for clinical research may make decisions very differently. Millennials may make decisions one way, but they have different considerations than people in their 40s or 80s. Can you touch on that a little bit and how that might change the informed consent process?

Kristina Wolfe

I think we all agree that shortening the actual form is needed. But from a Millennial's standpoint, the way I read things and review things and even respond to things is often quite different from someone else. I'm motivated by very different things than others may be motivated by, but that's *not* based only on my age. It's based on me as a person as well. And so I know we can't individualize the process every time, but that's where that human component becomes necessary. I think we can look at the language based on the populations that we're targeting for these trials, maybe different

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subpopulations or different cohorts with different informed consent forms or different processes. Maybe stratifying the way that we're communicating or going through the process with these different subpopulations that fall within the criteria that we're using. That's something to consider.

Mary Elizabeth Williams

I think it also comes down to who is designing the trials, who is writing the language: If everyone on your team is a 55-year old white man, how is that really going to speak to a 25-year old woman who is going to be enrolling in this trial. There has to be diversity at that side of things and diversity does not just mean racial diversity. It also has a lot to do with generational diversity and being able to speak in the language of your actual patient population because you come from that population, you represent that population.

Alyssa Lanzi

I think that's true. A lot of investigators have a different demographic than their patients. They can't help that. So it's important to include all stakeholders in the beginning when you're developing your protocol, when you're developing your documents. It's that idea of having all of the stakeholders on your research team from the beginning. We often try to have somebody with traumatic brain injury or somebody with Parkinson's disease actually on our research committee that develops this study with us. That's been successful for us to try to figure out how to enhance buy-in as well.

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—MARY ELIZABETH WILLIAMS

Lindsay McNair

With this discussion about how the informed consent process needs to be personalized, needs to be customized - I think the theory is, if you're choosing experienced investigators and experienced research teams, they should know how to do this. So they wouldn't be training, or as people have said when I suggested they'll get offended by the idea that that they should have training, because they've consented lots of people before. How do we provide better education to the study teams to better prepare them for thinking about these conversations or in a more personalized way?

Alyssa Lanzi

There's no doubt about that. I've now been at three different universities and every single time that's the first thing I do - talk to them about what the procedures are that they've typically done and their protocols. Then I give them suggestions. As I'm giving them suggestions, their eyes widen. "We've never done it that way before. I don't want to do it." I tell them to try and see how it goes.

For example, one of the modifications that we do in all of our consent forms is include pictures to describe the key components. We also include true and false comprehension check questions embedded within so that even if potential participants don't ask questions I can gauge if they're understanding everything that's being asked of them and then enhance my conversation with them.

Something else we've done recently that has been really successful:

There is always somebody on the team who's responsible for training research assistants or anyone actually doing the informed consent process with participants, and they have to go through like four different role-play scenarios with me. I act like a patient and ask kind of crazy questions and things like that, but it makes them feel confident and comfortable if these obstacles come in their way before they're actually in the room with the participant. And that training goes a long way because I've actually had them, those students, able to train other students. It builds their confidence. That has been really successful for us.

Audience member

Yes. I just want to take it back a little bit. We worked for a patient recruitment company, so we're right in the beginning of that process. We try to use language that doesn't make the patient feel like a passive vessel, but a lot of times we get pushback from sponsors or IRBs. How do we kind of walk that fine line between making a patient feel included and valued, but being sure we address those guidelines as well?

Lindsay McNair

The answer is probably the same answer that's always true in clinical research, which is, "it depends." Without knowing the examples of why people will push back it's kind of hard to say. I think the idea of using graphics and things like that is great.

Alyssa Lanzi

Always, always go always to the IRB meeting where they are discussing

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—ALYSSA LANZI

your study. It makes a world of difference. To build that relationship and provide the rationale to those who're doing your study as to why it is that way will help you for future studies as well.

And I know a lot of people are afraid to go to those meetings for a lot of different reasons, but it really does help. A lot of times they just don't know why you made those modifications; they have never seen that before. Simply saying to them something along the lines of, "Well, we do it this way because we had a patient with Parkinson's disease, and this helped them understand." That's a hard argument to go against.

Mary Elizabeth Williams

Just sort of breaking these ingrained patterns, right? In tech and journalism and media where it's like, "Well, all we ever want to do is disrupt," right? And it's like the whole thing you want to do is break things?

In healthcare, you *don't* want to break things. But the problem with that is the things that don't work get inherited and passed down from generation to generation to generation of doctors. When I see young doctors or young researchers reflexively adopting strategies and communication techniques that do not work, I think there's so much opportunity to push back. I think this is a very fearful industry in a lot of ways. It's hard to push back, but we have to. Any point of inflection where we can come in and say, "We have to try something different" is important.

"...always go to the IRB meeting where they are discussing your study. To build that relationship and provide the rationale to those who're doing your study as to why it is that way will help you for future studies as well."

—ALYSSA LANZI

And then the idea that you can't call a patient a person is bananas. Little things like that. The fact that nobody will say "die," right? Why can't we just say somebody died? There are so many opportunities to just be clear and less fearful that we're not taking, because we're afraid. But the way it's always been done doesn't work.

Audience member
I've always been perplexed: If we talk about patient-centered research, why are we still using the words "human subject?"

Mary Elizabeth Williams
That is not a friendly word. That is not a welcoming word.

Audience member
I mean we've talked about having this trust, and then we say "subject?" In Chicago, we are trying to do more with cancer trainees, working with them on their research designs, on how they communicate to patients. We haven't really touched on informed consent, so I would be interested in how you think research advocates or patient advocates could play a role?

Kristina Wolfe
A few pharmaceutical companies out there are proactively involving patients. That's why I was saying co-creation of these documents really does impact your recruitment strategy. It helps not only empower some of these patients that are brought into those conversations, but it can also impact how you engage and advocate for patients. Maybe

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—KRISTINA WOLFE

it's a matter of designing or co-creating the training materials with the advocate that spearheaded that initiative.

Alyssa Lanzi

I think it's discussing *why* you chose to do what you did, especially to people who weren't involved in our co-creation process. So yes, we hope we have this ideal team, that's all the stakeholders working together and then you develop it. But then we need to share with others of why we developed it that way.

I'll say to the research assistants, this is why this is in here, because we feel like that's conveying this message, or this is why we did this because these populations really attract to that. Having that rationale is important. I think we often think the people on the ground actually delivering that don't need to know the rationale. But I can see such a big difference when we also bring that goal-collaborative process and provide that rationale for the people who are actually delivering the informed consent process. That makes a really, really big difference as well.

Lindsay McNair

So going back the term "human subject." I think there's probably agreement that no one is in favor of that term, but it is still the term. It's unfortunate that it's used in the regulations that govern researchers, which is why it still gets carried over into a lot of language that you see in communications. And there is a resistance to calling people who are participating in clinical trials "patients" because we do want to make sure we're distinguishing between someone getting medical care from

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—LINDSAY MCNAIR

their treating physician, versus someone participating in a research experiment.

So what is the preferred term? [audience and panel vote]

"Research participant" wins by a landslide. Good. We had been trying to switch our verbiage on that as well. Moving away from the subject terminology that we've been conditioned to for a lot of us who live in highly regulated environments and moving toward "participant" as a term that much better respects the equal role of the patient. The equal role that participants have as part of the research enterprise. A subject is something that is studied. A subject is a passive thing, a participant is an active thing.

Any last comments from the panel?

Alyssa Lanzi

Sharing the success stories: I think there're a lot of success stories out there when it comes to the informed consent process. We spend a lot of time talking about what doesn't work well. We need to start talking about what is working, and what are some suggestions, and why it is working as well. So, trying to figure out some creative ways of sharing those so we're not always re-creating and re-inventing the wheel.

Kristina Wolfe

This is for the biotech and pharma companies: Maybe invest in developing those relationships with your sites, and then empower the

"A subject is something that is studied. A subject is a passive thing, a participant is an active thing."

—LINDSAY MCNAIR

sites to invest in the patients that you're recruiting for your studies.

And I'm going to push back on the "research participant" name. I don't like being defined by anything, let alone a disease I live with. Maybe we can start thinking a little bit more creatively about "research participant" and instead encompass the whole person as a part of this process.

Mary Elizabeth Williams

Seriously, "person" is a fine word. We don't have to make it harder. And it's like when people say, "Well you don't want to say you 'battled cancer,' so what should I say? And I say "You can actually say I had cancer. You can say I was treated for cancer. That's fine."

I would want to also add on the other side of that, not just sharing successes, but I think every person in here who is a patient is here because they are a squeaky wheel. And good for us for being squeaky wheels, but the big conversation cannot be defined by the squeaky wheels among us. We also have to be really working a little harder and pushing a little harder for the person who may just be blindly signing the consent form - who may just not be asking the questions. And we need to really be looking more closely at those people because they are the ones who need the most help. We can often figure it out for ourselves, but the ones who aren't complaining are the ones who need it probably the most.

"...invest in developing those relationships with your sites, and then empower the sites to invest in the patients that you're recruiting for your studies."

—KRISTINA WOLFE

Key Learnings

Enhance patient confidence by ensuring true understanding of the consent process

Informed consent needs to become a more patient-friendly process with improved understandability at the forefront. The focus remains on the completion of paperwork, often without considering if the language being used is patient-friendly. We need to better make sure that patients truly understand what they are consenting to.

Reconsider language used in conversations and patient facing materials to build trust

“Subject” doesn’t inspire confidence in patients. Because it is used in the regulations that govern researchers, it often gets carried over into patient-facing materials and--worse--into conversations. There needs to be work from all sides to improve the language used for research participants. Patient input on preferred language would go a long way to bridging the confidence gap.

Overcome “unfriendly” language by meeting with IRBs to accelerate change

Patient-centric language is often at conflict with established clinical research guidelines. Meeting with IRBs is important to progress. Attending IRB meetings and explaining that certain patient friendly language helped patients better understand the consent process would go a long way in spearheading change.

Key Learnings continued...

Improve the patient centricity by training study teams on new patient-centered procedures

There needs to be further buy in from site teams. Sponsors have a significant role in developing relationships with sites. Empowering sites to invest in the patients that they are recruiting would go a long way in creating a more patient-centric consent process. Further training for site teams on procedures and protocols would improve patient understanding and trust.

Cultivate trust in minority communities by involving members of those communities in study design

It's important to involve people within from the communities that are being targeted in trial design and communications. If everyone on a study team is a white male in their 50s, how will they speak and connect with a Latina woman in her 20s? The ability to connect on a human level with patients is exceedingly important in generating trust and understanding from a community.

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