Transcript

Adrian Hernandez

Welcome to the NIH Pragmatic Trials Collaboratory Podcast, where we discuss the latest knowledge and best practices in pragmatic clinical trials. I'm Adrian Hernandez, Co-PI for the NIH Collaboratory, and one of the moderators for this series. You can find a full list of episodes at rethinkingclinicaltrials.org/podcasts. Thanks for joining.

Hi, I'm Adrian Hernandez, one of the PIs for the NIH Pragmatic Trials Collaboratory. And today we're joined by Emily O'Brien, who's here to discuss her recent Grand Rounds presentation, "Avoiding the Fumble: Building on a Decade of Lessons From Pragmatic Clinical Trials." Emily, thanks for joining us.

Emily O'Brien

Thanks so much for having me, Adrian. You know I love this topic, I know it's close to your heart as well.

Adrian Hernandez

So, first of all, like, this is an interesting title. I never really thought that football would go together with clinical trials. So, what do you mean by "avoiding the fumble?"

Emily O'Brien

Yeah, well there, there are actually a lot of common themes that could probably be a full presentation that kind of connect the Collaboratory and pragmatic trials to football. And the fumble is just one of them. But obviously, you know, both require teamwork. There's a certain level of specialization for all the team players and they really have to work together.

But the concept of the fumble, really, I think has been an interesting way to acknowledge that we don't always get things perfectly right the first time. And part of the goal of programs like the Collaboratory – and some of our other projects that focus on team science and metascience and pragmatic trials – is to learn from those and to do better and to hopefully better anticipate challenges and work together to overcome

them. So, the fumble seemed like a good way to illustrate what we're, we're hoping to avoid and think about how we can work together to achieve that.

Adrian Hernandez

And it sounds like, just like great football teams have a terrific playbook and a practice and plan, that's a possibility for clinical trials. And you're pointing to other industries that have a much better approach in terms of what they do, ranging from banking to airline travel.

How are you thinking about those other industries and how does that translate to healthcare and trials?

Emily O'Brien

It's really interesting to think about. And this has been a topic of conversation for several decades now, going back to conversations that started around the learning healthcare system or learning health system in the mid-2000s and sort of looking around to the way that we do things in healthcare and saying, there's some things that really could benefit from some improvement.

And I'll just give one example. So, this is from a NASEM report where the author said, "If airline travel were like healthcare, each pilot would be free to design their own pre-flight safety check or not perform one at all."

And so, we sort of look at the areas of opportunity in healthcare and there's certainly many on the operational side. You know, as scientists, what we're hoping is that through data and through doing research in clinical care settings, that will not only help us to generate evidence to improve care, but also to learn as we go and to share how to do those trials better with the research community.

And so that's sort of the vision of the learning healthcare system. And what's been exciting about the past 20 years is to kind of see that vision come to life in different ways. And also to, you know, take the lessons learned from those decades of experience and begin to implement them into the next studies that we're, we're doing and begin to train students and clinicians in how to apply those well.

Adrian Hernandez

So, how would you describe the current state of affairs for clinical trials right now? Are we fumbling?

Emily O'Brien

You know, I, I think we'll always be fumbling a little bit. I think we've moved in the right direction in terms of the number of fumbles and the type of fumbles. And so like, when you think about something like data, for example, some of the sort of early progress was on some very, very basic things like just being able to query age and gender across multiple systems, for example.

And, you know, that was an important foundational piece that we had to have in place before we got to more complex efforts involving things like AI and natural language processing, which is where a lot of the work is focused today. So, I would say, you know, we've hopefully gotten a lot of the sort of silly mistakes out of the way and are now beginning to think more about kind of how to optimize the way that we're doing things in the setting of pragmatic trials.

And what's been interesting to learn through the Collaboratory that I also touched on in the talk is that a lot of this does come down to people and having the right people within the healthcare system on board with what we're trying to do as scientists.

And, you know, if they don't buy into this concept of a learning health system and don't think that there's really motivation to do things differently, that's where a lot of progress gets stalled. And so, I think a lot of those relationships have developed over time and have begun to really show dividends in terms of progress for how things can get done and get done more efficiently within these systems.

Adrian Hernandez

You spoke of the researchers and trying to be a part of the learning healthcare system. What about the disconnect, you know, with healthcare systems? So, aren't there two different audiences that we're having to address through these embedded trials? And are the researchers the right ones leading the way? Is it the healthcare systems? What's the answer?

Emily O'Brien

Yeah so, there's a great quote that we use over and over in the Collaboratory about researchers having this tail wagging the dog problem. Where we kind of drop in and we

think something's a great research idea and “Ah, this is gonna answer some critical question that's gonna improve health and outcomes for everybody in some area. And surely the health system will be on board with this and will want to collect data and help us answer this question.”

But the health system has, you know, its own priorities. And its number one priority is to deliver care and to get paid for that care and, and to do it in a way that's safe and, and effective and increasingly that optimizes patient satisfaction to the extent that it can.

And so, we see those goals as complementary to what we do in research, but it is also true that for people whose day jobs focus primarily on, you know, clinical operations and care delivery, they may not be as hyper-focused on having, say, structured data elements that are all in the same format so that we can use them as researchers on the back end.

And so, a lot of the progress with respect to relationships, I think, is getting them to sort of buy into that vision and being able to think about our own questions in a way that minimizes the burden to systems so that they can still do what they need to do, but we can also help them to get the answers that they need and then to share those lessons more broadly.

And so, I think we'll be working toward that vision for a really long time, just given the constraints on resources in healthcare. But it has been gratifying to see the stronger connections and, I would say, better alignment in the way that we think about how research and healthcare are connected over the past 20 years.

Adrian Hernandez

So, as you and others have looked at all the fumbles in clinical trials, you've put together a playbook. Tell us a little bit about the Playbook and the overall goals of the Playbook and what's in the Playbook.

Emily O’Brien

So you think about a football team, like – the goal of course is to win, right? And so, you want success. But you need to know who's going where, who's doing what. It needs to be developed in a way that acknowledges the limitations of the system and the resources available within the system, you know, just like the playbook has to respect the rules of football and, you know, the limitations of the athletes that are on the team.

And so, we see the Playbook as really the pragmatic sort of application of a lot of the principles that we've talked about in the Collaboratory and other venues about, you know, how to do pragmatic clinical trials well.

And many of those sort of best practice recommendations sound really great in theory. And we've heard over and over again that people run into different realities when they try to apply them in real life. And so, the goal is to give people strategies to implement the sort of high-level vision.

And then, what I see as a critical contribution is encouraging them to be transparent when things don't go according to plan and to say, you know, we're gonna watch the tapes, we're gonna learn from past mistakes. And that'll help us to better anticipate what's coming and how to do things better the next time.

And so, we try to give like the basic building blocks, but also point to case studies that illustrate like how some high-level plan or vision to answer some question or improve care in some way, like, what does that actually, what did that look like in reality? What worked well, what didn't work well?

What would the investigators say to someone who's just starting out trying to do the same thing. So that they can, you know, hopefully avoid their own fumbles and then do the same sort of education and dissemination of their lessons learned when they're done.

Adrian Hernandez

And this playbook is really designed to leverage PCORnet. What's unique about that? And why do you even need a playbook?

Emily O'Brien

We have had a lot of interesting discussions with people who we would say are PCORnet naive and are, like, sort of aware of the network but haven't really worked with the network. And what we heard from investigators who might be interested in using the network's resources for research is like, "This seems great, but I don't really know where to get started."

And so, some of the advice is more tactical. Like, "Here's what the process looks like to do a feasibility assessment," for example. "Here are the people that you wanna contact to get started." To try to make it, like, super easy to get connected with those resources.

But then, the other part of it is, what I see as, like, really more generalizable strategies and best practices for doing pragmatic clinical trials and pragmatic research well, no matter what data resource or network you're working with.

So, these would be things like, best practices for patient engagement; you know, how to think about data access when you're working with multiple sites who might be mapping their data to common data model. And so, some of it is PCORnet specific, but I think a lot of the principles that we talk about in the Collaboratory for how to do work in this area well, those shine through too.

And hopefully it'll be useful for other projects that investigators are leading even if they're not directly connected to PCORnet.

Adrian Hernandez

This is tailored for any type of investigator. Is that right?

Emily O'Brien

Right. So that is a unique aspect of the Playbook. As you know, there's been a big, a big shift over the past 10 or 15 years to what a conventional research team looks like. And this is great progress, you know, from the perspective of people in organizations that are trying to push patient-centered research forward.

There's the "nothing about us, without us" kind of mantra that says, hey, like, we can't just have investigators who are coming in and proposing ideas totally independent from the patient communities and the family communities that they represent. Those people need to be at the table.

And so, the goal for the Playbook was to make it accessible both to the science community, which has their own quirky language and terminology that isn't always accessible. But then also, people who have questions that they think need to be answered about a condition that they have or their family member has or that they care about.

So, we tried to write it in a way that would make it clear how PCORnet might be useful, you know, even for, for people who are kind of just getting started with research or maybe think that PCORnet might be a good starting place to answer a research question but aren't familiar with the process of sort of getting that going.

And so, the, the goal is really to like, keep the barrier to entry really low. And then hopefully direct people to the right place so that they can get started, even if they don't already have lots of connections within the research community and haven't been part of a study before.

Adrian Hernandez

The Playbook's inspired by the Living Textbook, as I understand. So, is the Playbook gonna be a, a “Living Playbook?”

Emily O’Brien

That's the goal. We've seen a, a huge explosion in interest in pragmatic clinical trials. And, along with that, I think often comes some reality checks that people have to confront as they begin to understand like, what it really takes to, to do one of these studies well across multiple sites.

And so, I think, you know, the, the good thing is we're gonna have more people who are doing this kind of work. And, if we can establish a culture of transparency and sharing, I think that can really accelerate the implementation of best practices and refinement of those practices, as well as the type of investigators who might wanna be involved in this, in this work.

And so, really the, the goal is, is to broaden the community and sort of broaden the opportunity for, for people even if, you know, they're, they're newer to trials or come from a sort of conventional explanatory trial background to really show them the power of this work. And then to give them the tools that they need to get started and to do their, their work well.

Adrian Hernandez

Where can people go to find the magical Playbook?

Emily O’Brien

They can go to the PCORnet website. And if they go to the PCORnet website, they'll see a Playbook link under the resources tab. And once they get there, they'll see that it's broken down into modules, which they can think of as chapters, that cover different topics like “Getting Started” and “Dissemination.”

And we'll be adding to these over time. So, we have one on engagement that's coming out soon and another one on case studies that illustrate the soup-to-nuts approach to different types of questions within the network. And so, they'll find a, I think a lot of useful content.

They can also download that content and save it and have that accessible wherever so they can, you know, reference it and use it. And then they'll see some things like videos, quotes from investigators, outside links to other resources that are helpful for pragmatic research.

And we are super, super eager to get feedback on what people like about the playbook and areas that we might wanna focus on in the future. So, there's also a mechanism for feedback where people can tell us what they think. And would love to, to hear from folks.

Adrian Hernandez

Terrific, Emily. Thanks for sharing your insights about how *not* to fumble in pragmatic clinical trials and developing the Playbook for everyone else to follow.

Emily O'Brien

Great. Thanks for having me.

Adrian Hernandez

If you're interested in hearing more firsthand perspectives on pragmatic clinical trials, join us next month for another episode of the NIH Collaboratory Podcast.

Thanks for tuning in to this episode of the NIH Pragmatic Trials Collaboratory Podcast. You can find other resources related to conducting a pragmatic clinical trial on our website, rethinkingclinicaltrials.org. We look forward to seeing you next time on the NIH Collaboratory podcast.