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 Rich Platt, Hayden Bosworth and Greg Simon to discuss their *JAMA* Viewpoint, "Making Pragmatic Clinical Trials More Pragmatic."

So first of all, there's a lot of interest around pragmatic trials. And Rich, I want to turn to you first. So like, what are pragmatic trials and then what are the problems we're aiming to solve with them?

Rich Platt

Pragmatic trials occupy an interesting space in the clinical trials universe. They are trials that try very hard to replicate the conditions that will exist in actual practice. And they're often embedded in clinical delivery systems. So, on the one hand they're supposed to be rigorous trials intended to create generalizable knowledge, but to do that using the clinical settings that depend on existing infrastructure. So, marrying the scientific aims to the delivery system environments in which they work is the real challenge.

And part of what we, what we addressed in this piece in *JAMA* was the fact that we have observed over the life of the Collaboratory that there is considerable number of situations in which there's a mismatch between the outcome of the trial and the decisions that the host delivery systems make then about whether or not to adopt the findings of the trials. So that was the nettle that we tried to grasp.

Adrian Hernandez

And Greg, so as Rich was noting, these trials are aimed to be closer to the real world, embedded into healthcare systems. Is that an oxymoron? Is it possible to actually do a clinical trial inside of a healthcare system that's really directly focused on healthcare?

Greg Simon

Well, I don't think that there's any fundamental conflict between rigor and relevance. As Rich was saying, our goal is to bring scientific rigor to questions, but to produce information that's relevant to people who make decisions. And our job in that partnership when we're working with healthcare systems is often, you know, we are the people who do rigor.

You know, we bring expertise about methods, we bring expertise about what's the most rigorous way to answer questions. We do have to admit though that we're not the deciders about relevance. Relevance is what our customers decide. Our customers are the health systems or policy makers we want to inform. And when it comes to relevance, we should be learners, not teachers. We need to listen to our customers about what's relevant.

Adrian Hernandez

Wow. So, investigators may not be the customers here.

Greg Simon

I think one of the problems with our evidence generating process is that we often act – by we I'm pleading guilty to being a researcher and a sometime academic – we may think that our customers are grant review panels or maybe journal editors. And, unfortunately, those may be our short-term customers, but those are not our ultimate customers. Our ultimate customers are people who have to make decisions about healthcare.

Adrian Hernandez

So, Hayden, you spent a lot of time in implementation science and trying to change behaviors in sustainable ways. What do you see as the challenges in terms of pragmatic trials and healthcare systems and behavioral change?

Hayden Bosworth

I see two, two problems. One is a disconnect between the learner and the customer in the sense of timeline. So, we don't have all the results, right? But on the other hand, if we wait until all the results are in hand, we probably are not gonna have the customer in the end really engage with us. And so, there's this disconnect between getting them to adopt the project or program and then sustain something that's beneficial.

So, I think that there's that problem, there's this temporal order issue that we do need to have the system on board. So, working together in kind of a community is crucial. But what we find and what we reported in the paper was, there's this inconsistency where there were things that were not significant but yet were picked up and being used. Similarly, there were things that we would've expected that were truly effective and weren't being adopted and used. And some of those projects were so complex that it wasn't surprising, even though they were effective, that they weren't picked up. So, I think the holy grail is to take effective programs that are embedded and can be used in the healthcare system with their support and then sustain that program.

And we also have to kind of change the mindset. A five-year grant is wonderful, but the reality is that we know the customers don't have, they may only have three to six months. And so, we're really working with a very misaligned temporal order that we really have to think through a little bit more carefully.

Adrian Hernandez

And, you know, some of the themes that are in this paper, this Viewpoint, is around introducing flexibility in terms of evidence trials require. What do you mean by that? What do y'all mean by flexibility and the level of evidence trials require?

Rich Platt

Let's go back to Greg's comment about who's the customer. Often in order to obtain funding for a pragmatic trial, one looks to funding agencies that ask for a high level of confidence in the result. Statistically significant results of $p < 0.05$. Whereas the delivery system leaders are not nearly so interested in getting a particular level of significance. They would ordinarily say, if we can be moderately confident that a result is valid, then we'll adopt it because it's better than our making up a course of action all on our own.

And that tension is a pretty palpable one. And has a lot of implications in things like, how long does this trial have to run? As Hayden pointed out, delivery systems almost never have as much time to allow a trial to run to completion and produce a result as we or ordinarily look for. Or that we typically have funded in the Collaboratory.

Adrian Hernandez

Really interesting point there. And Greg, I wanna turn to you 'cause you've, I know you've had your own interactions with your healthcare system. And also, you know, as part of the Collaboratory, different healthcare system leaders. Do you experience or hear about healthcare system leaders rejecting an idea with evidence that came back with a p value of 0.06? “Sorry, that's not good enough. I'm just gonna go ahead and not do it. Come back when you have something more significant?”

Greg Simon

Well, I think, in my experience, your healthcare system leaders often, you know, trust their research partners to tell them – and some of them may even, you know, adhere too rigidly to $p < 0.05$. Sometimes our job is to tell them, you know, it's a little more complicated than that, but I think they trust us on that. When it comes to outcomes, what I hear more often is that healthcare system leaders are considering a broader range of outcomes. We are often required to declare one primary outcome measured in a particular way, and to declare a trial to be a positive or a null result based on that single thing. And healthcare systems care about more than one thing.

They care about clinical outcomes for sure. They also care about how much things cost. They care about how it affects the satisfaction or retention of members or patients. They care about how it affects the satisfaction of their staff. Whatever the current buzzword is, whether it's the triple aim or the quadruple aim, those things are buzzwords, but they're also real. Healthcare system leaders do care about those.

When we talk about rigor and relevance, all of those outcomes are relevant to healthcare system leaders. Unfortunately, sometimes we don't have very good rigor in those other areas. And what you hear sometimes, for instance, you're talking to healthcare system leaders and

their perception of participating in a trial is sometimes, "Our people really liked this, therefore it's a good thing and maybe we should do it."

But where they get the data for "our people really like this" is three anecdotes. So, I think as pragmatic trialists, we need to think more about how do we bring rigor to those other outcomes. Interestingly, you know our healthcare systems we work with are constantly measuring member and patient satisfaction. Often, they're measuring staff satisfaction or staff engagement or whatever the buzzword is for the surveys that all of us fill out in the healthcare systems where we work. We often don't think about those things as relevant outcomes to our trial, but we ought to.

Adrian Hernandez

Yeah. Wow. One of the things you're also pointing out is that, you know, often healthcare system leaders are having to make decisions without any data at all. And they need to do something in a timely manner. So having important and impactful data, their view may be different than what a typical journal would be, or peer review.

And so, Hayden, one of the things that also comes out in this piece is essentially you gotta plan for success. You know, shorten the duration of planning and implementation. I know you've talked about those kind of themes in the past. What were y'all meaning by shortening the duration of planning and implementation? I always thought, the longer you plan, the better you are. But it seems like the argument is the other way.

Hayden Bosworth

There's this dilemma, right? You know, more planning, better outcomes. But again, I think that in the end, as Rich and Greg have clearly stated, we have to reflect who our customers are in this context. And so, most of us as researchers probably live in worlds where we're doing traditional academic research. Where trials, you know, drug trials, those are gonna be very different than I think when we're working with healthcare systems and they're embedded. And understanding their needs, which are gonna be probably completely opposite in those situations. And so, I think of the people I work and train with as, you have to be able to work in two worlds. And that world is traditional, maybe academic, federally funded where you have that luxury. But the long-term tale of sustainability is there, but it's not the focal point.

Whereas when we're working in the embedded world, we don't have that luxury. We really have to think about how we can do this more quickly, more efficiently. How do we know that we have an indication that this is working, but it's not perfect. But we can still maybe get it out there. And build the car as we're moving down the road. But the car is there, has four wheels. And maybe that's the way we need to think about it when we're working in this context.

Rich Platt

You know, Adrian, I think one of the other things that your question brought up is, before you get started, it's important to understand whether success would mean implementation, adoption by the host system. And one of the major reasons that this might not happen is that whatever we're doing is an added cost. And that should be, it's important to confront that right at the

beginning. Because if the intervention is not gonna be sustainable at an economic level, then it really calls into question the value of doing a trial.

There are plenty of other things that get in the way of sustainability. The environment that exists at the end of a trial is gonna be different from the environment that was true at the beginning of a trial. Even if it's a pretty short trial. So, there's lots of other stuff that can get in the way of adoption. But in our experience, we don't always think explicitly about whether an intervention is going to be sustainable after the trial is over.

Adrian Hernandez

Right, right. Alright, as we wrap up, I wanna turn to each of you to share your views on, what's one or two things that we could change. Rich, I'm gonna give you the last word here, since we started with you. So, Hayden, what's one or two things that if you had the magic wand, you would change?

Hayden Bosworth

Allowing the customer to define what success is and to think about sustainability as early as possible if you meet those criteria for success.

Adrian Hernandez

Greg?

Greg Simon

I'd say at a minimum, you know, applications for funding should declare who's my customer. In a perfect world, a review panel would include some of those customers.

Adrian Hernandez

Ah, excellent. Rich?

Rich Platt

It's important to be light on your feet. It's often the case that six months or a year into a trial, it's clear that something ought to be different to maximize the chance of some kind of success. And it takes real effort and sometimes courage to change a plan that many, many people have already signed off on.

Adrian Hernandez

Yeah, no, that's especially important, so. Just thinking about the lifecycle, these programs have taken two years to develop and apply, five years to conduct, and often even delays in reporting

out a seven-year life cycle doesn't necessarily translate into improving healthcare as a learning healthcare system.

So, thanks a lot for spending time with us on this podcast. Hopefully everyone enjoys learning about making pragmatic clinical trials more pragmatic. If you're interested in hearing more firsthand perspectives on pragmatic clinical trials join us for our next 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.