Adrian Hernandez:

Hey, this is Adrian Hernandez and welcome to the NIH Collaboratory Grand Rounds Podcast. We're here to give you some extra time with our speaker and ask them the tough and interesting questions you want to hear most. If you haven't already, we hope you'll watch the full Grand Rounds webinar recording to learn more. All of our Grand Rounds content can be found at rethinkingclinicaltrials.org. Thanks for joining.

Wendy Weber:

Hi, this is Wendy Weber. I work at the National Center for Complementary and Integrative Health at the National Institutes of Health. Today we're here with Lesley Curtis, Patrick Heagerty and Keith Marsolo, who will be reflecting on the EHR workshop series, advances at the intersection of digital health, electronic health records and pragmatic clinical trials. Just as a little bit of background, the Healthcare Systems Research Collaboratory started holding an annual workshop in conjunction with our steering committee meeting in 2016. We've had discussions about ethics, dissemination and implementation, A versus B trials, as well as design and analysis, all of pragmatic trials. This fifth workshop advances at the intersection of digital health, electronic health records and pragmatic trials, was recently converted from an in person meeting to a grand round series that was conducted over the last two months. We had a series of moderated panel discussions talking about the use of digital technologies and pragmatic trials. Some lessons learned from some of the collaboratory demonstration projects and how existing data structures and platforms could be expanded not only for conducting pragmatic trials, but for rapidly disseminating evidence and information to relevant decision makers.

We started off on May 1st with our keynote from Dr. Califf talking about whether or not the COVID crisis could lead to reform of the evidence based evidence generation system. We then were followed on May 8th with a panel moderated by Patrick Heagerty, looking at real world evidence and non traditional electronic health records. On May 29th, we had a session that I moderated talking about the experiences from Collaboratory pragmatic trials, and then on June 26, just last week, we finished up with a panel session looking at keys to success and the evolving electronic health records environment that was moderated by Keith Marsolo. So Lesley, you moderated the first keynote session with Dr. Califf, what are some of the highlights from his presentation that you want to share with everyone?

Lesley Curtis:

Thanks, Wendy. It was a great way to start the workshop series, wasn't it. So, Dr. Califf made several points, three of which really stuck with me. The first was just noting what has been truly a rapid acceleration toward virtual designs or hybrid kind of combination designs during this COVID pandemic. Really moving quickly toward direct from patient data collection, which is something we've talked about for a long time, but to see such rapid movement in such a short period of time has really been striking. He also made a point really directly relevant to our workshop series topic that the ingredients for interoperability and access to health records, they exist and they have existed, putting them together is what remains a problem. And gave a few examples of where we've seen those challenges arise again in work, moving in this COVID pandemic era.

And then the final point that really stuck with me was how, if we use digital information, whether that be electronic health records, tele-health or apps, if we use them effectively, we should be able to free up effort, human effort, right? To address the really important human components that often hold us back in research. So those are probably the three big takeaways that I had. It was a rich discussion after his talk as well.

Wendy Weber:

Yeah, it was really interesting talking about where we could go and how fast some things are moving right now with really transforming how quickly we can generate evidence. Patrick, you led the first panel discussion with some of our experts talking about real world evidence and non traditional electronic health records. What were some of the key takeaways you had from that presentation?

Patrick Heagerty:

Yeah. Thanks Wendy. First I want to say the speakers for that session and their topics, and then I'll give some comments from my perspective. We were really fortunate to have Jacqueline Corrigan-Curay from the FDA. Who's the director of CDER's Office of Medical Policy. And she set the stage by talking about real world data as a building of the foundation, and then expanded on that with respect to generating real world evidence. And then Josh Denny who's now the Chief Executive Officer of NIH's all of us research program. He presented a different angle, which was really around how to leverage clinical data to advance discovery. And so that was really exciting looking at the multiple sources of data that we have available clinically, and then how to combine them in ways to characterize a person's health status, often called phenotyping or clinical phenotyping or electronic phenotyping. And gave really wonderful examples from his experience at Vanderbilt, doing science, leveraging those multiple sources of data.

I think for me the highlights that really stood out for me was Dr. Corrigan-Curay, she did talk about the foundation around data standards, but was really wise to articulate after that comes research, design and analysis and ultimately evidence. And so when we talk about real world data, we often think about observational data and the context is observational for EMR data, but the study design is frequently randomized, like many of the trials we've done or almost all the trials as part of the Collaboratory. So I really liked that reminder, real-world data can be coupled with randomized designs. And she did set the stage for the variety of clinical data sources that are available, including, as Leslie mentioned, digital sources and how we look future oriented towards leveraging those opportunities. And then Josh Denny, I think gave wonderful examples of how we can try and sharpen our measurement using electronic data sources. Sharpen that by combining the data sources and then actually thinking creatively about how to use those data sources ultimately to make a phenotype.

But oftentimes it's kind of a predictive phenotype and so we can retain the richness of the score that may underlie that predicted phenotype. So two really well received talks, really nice summaries of where we've been and then a vantage for where we're going.

Lesley Curtis:

Great. Thanks Patrick. And Wendy, I'd like to actually turn to you and ask you to share your reflections on the panel that you moderated. Really highlighted what we've learned and what the collaboratory demonstration projects have learned.

Wendy Weber:

Yeah, sure thing, Lesley, we were quite lucky to have four of our pragmatic trial PIs join us to talk about some of the lessons they've learned and hopefully help people to address some of these similar issues as they're thinking about designing and conducting other trials in electronic, utilizing electronic health records or trying to embed these studies into healthcare systems. So as I talk through each of the speakers, I'll give an example of my key takeaway from each of their talks. So Dr. Jeffrey Jarvik from the University of Washington talked about the LIRE study where they did a trial in patients with back pain. And one of the things that they really leveraged was the electronic health record, both for diagnostic

information, but also for procedural codes. And that when you're doing that, he talked quite a bit about really needing to understand how those codes are used. In this trial they were working across multiple healthcare systems and the reality that there's really important information in how those codes are used differently across sites.

And that you really need to understand how those codes are used before you just pull the data using those codes, so that you're really able to combine the information across sites so that you're actually using similar information, even though the codes may be somewhat different, based more on culture or context of how things are coded in one particular healthcare system. So I think that was really useful for people to think about. I think a lot of times we hear from the community, oh, the data is all there you need just have to pull it. You have to understand how the data is being coded into the system to really be able to utilize it well. And then Lynn DeBar also joined us from Kaiser Permanente, Washington Health Research, and she ran the payback study done across several different Kaiser systems. And she really talked to us a lot about the leveraging and using patient reported outcomes that might be part of the electronic health record and really being able to understand and look at different strategies when that data isn't as routinely collected, as you might hope it to be for a research study.

And what are different effective ways to augment those patient reported outcomes. And I think as part of her discussion, one of the things she talked about was this idea of, might we want to think about uncoupling the collection of those patient reported outcomes so that they're not always, or not only collected at the clinic visit. Because patients may be slightly different when they need to schedule a visit to see a clinician versus when they're functioning potentially much better at home and not needing to come in for a visit. And I think it sparked a pretty interesting conversation to think about what's the pros and cons of potentially uncoupling those data collections. And then [inaudible] joined us also from the University of Washington School of Medicine to talk about the TCO study, which is done across trauma centers. And I think he had one of these big key take home messages, which was really about, if you really want to do a pragmatic trial, there are a couple of things that can really make it difficult.

And one that he said that if you want to design a pragmatic trial for success, select an endpoint that's already routinely collected in clinical care, that will be informative. And the other is run your trial and collect your outcomes in a way that does not impede clinic workflow. And that if you can accomplish those things, you have a much higher chance of success in completing your trial without as much missing data. And I think those were really good suggestions and recommendations that he certainly learned in doing his TCO study. And then finally, Vince Mor from Brown University School of Public Health. Talk to us about the proven trial. And I think he provided just this really elegant example of how to go beyond maybe the data that you might only think you have access to initially and in the healthcare systems that you're partnering with, which in his case was nursing homes.

And because he was working with an older adult population, they actually went and looked at the centers for Medicare and Medicaid services data, through their virtual research data center to actually be able to capture much richer and much more complete data on health service utilization and even mortality. And in a way that was quickly available, which really for him, he's described it as a game changer to be able to do research in that population. There are some limitations, including not being able to get data in nearly as quickly on Medicare advantage participants, but that thinking about where else can you get data, what Patrick was talking about with the previous panel, just expand the completeness of the data that you have on your participants work and you look for those linkages, I think was a really insightful lesson that Vince brought to everyone.

Lesley Curtis:

That's an excellent summary, Wendy, and you've highlighted really so many of the specific learnings from Collaboratory projects that are really generalizable to the next set of pragmatic trials. Keith, I'd like to turn to you and maybe hear from you your reflections on the panel that you moderated that was focused really on what those keys to success are in the ever-changing EHR environment.

Keith Marsolo:

Sure. Thanks, Leslie. So I think there was a lot of great learnings. It was a great set of speakers. And so what I was struck by was, so we had Dr. Rachel Richardson outline how each of the Collaboratory projects are leveraging the EHR. Whether it was in terms of determining eligibility for patients, delivering an intervention or the ascertainment of outcomes. And obviously the trials would be using one of those, but I think what I was, at least one of those, but what I was struck by is almost 60% of the studies in the Collaboratory, were using the EHR for all three components. And so I think that really demonstrates the potential and then it is a great opportunity learning best practices and what to do and what not to do. And so in that spirit, we had Dr. Holt Oliver, outline several of the challenges that his team faced in completing the ICD pieces trial. And a lot of real practical suggestions on how to address them.

I think we tend to get hung up on whether the data are in the EHR or not and how things are coded and so forth. But he actually was describing some of the more practical things that need to be faced such as, if you've got a trial that's running over five years, how do you deal with EHR upgrades and staffing changes? And so if you expect that an analyst may stay at a site for a year or two on average, and you've got 20 sites in five years, that could be a fair amount of turnover. So those things seem to be mundane and it's not necessarily what you would normally think to plan for. But I think he really stressed the importance of having that kind of planning in place so that it doesn't jeopardize the potential completion of your trial. And then we had Dr. Chris Longhurst describes a future version, future vision, excuse me, of how we might use the EHR to support pragmatic research. And then I think specifically in the context of really more of a learning health system.

So I think building on some of his previous research where they talked about the concept of a green button, if you will, where you could pull up, if you had a patient, you could pull up and say, what are some of the outcomes of similar patients so I would know what to do? So it's great for identifying potential treatment, but I think what he really highlighted was there's lots of areas where we have gaps and specifically around things like COVID and what treatments should use. And so I think identifying those gaps and then rapidly starting new trials to help determine effectiveness, I think it's a really powerful use case. And I think it hints at what's possible. So I think as we've described, the challenge with EHR based research has always been an issue of scale. And so it was really great to hear from Dr. Theresa Zayas-Cabán about what the office of the national coordinator is doing to really identify in advance research priorities as they relate to health IT.

And I think there's been a lot more movement in recent years about adoption of standards through legislation like 21st century cures. And so I think as these priorities get picked up by the EHR vendors and adopted across the industry, I think that should go a long way towards simplifying the startup and the conduct of these EHR based pragmatic trials.

Lesley Curtis:

Yeah. That was a great summary Keith of a really rich set of presentations. You touched on a few things that I think raised a broader question, maybe that I'd like to ask some of the other moderators to weigh in on as well. And that is, I guess we think back to the beginning of the Collaboratory, what do we think

some of the key advances have been, especially in the EHR space, and do we have a prediction about what the future big challenge might be? I don't know, Wendy or Patrick, any thoughts about that?

Wendy Weber:

So this is Wendy. I can speak a little bit from the funder side. I think one of the big challenges we continue to face is working across different health record systems. I think we're getting better, but I still think it's challenging and certainly ox ability to have some consistency across programs and having some similarities. But when the EHRs are built to allow customization, it makes it more difficult to combine across different systems. And so, as a funder, I think that's one of the things that we hear most often in peer review and challenges and questions that people have when there's an idea that you're going to combine data across electronic health records. I certainly think it's possible, but it's not as easy as I think most of our investigators have figured out how to do this. But it's much more work than I think some people initially believe coming into this field. Patrick or Keith, what do you guys think?

Patrick Heagerty:

Yeah. Wendy, I'll add to that just briefly measurements and quality measurement is at the core of all science. And I think we've learned to be really careful to understand the measurement we're obtaining from the medical record. And to figure out how best to use it, to understand when it's fit for purpose and when it's not. And then I think looking forward, we'll continue to expand our ability to get quality measurements, either through standardization efforts or through direct participant technologies. I think there's a lot of excitement around that. So great reminder that quality of measurement is at the core of all we're doing.

Keith Marsolo:

And I think maybe the only thing that I would add to all of that is the things that you would try to measure on patients. In many cases, particularly for pragmatic trials, those are often things that you would want to know about in order to provide patient care. And so I still believe that as we move towards trying to use artificial intelligence in healthcare and precision medicine and things of that nature, those algorithms and activities are best served by having high quality, reliable data on patients. And so I do think that the types of features in the EHR that we need to support that are the same things that we need for the actual trials. And so I'd like to think that we're moving towards a convergence there.

Wendy Weber:

That's great. One additional question that came to mind for me as I was reflecting back on all of, sort of relying on the electronic health record and digital capture of a lot of this information is, in these pragmatic trials, there's always this tension and balance between trying to be as minimally invasive as possible, and still do the experiment and trying to get really high quality data like you were talking about Patrick. And I think we often will bring up the pricey wheel as that continuum between the explanatory and the more pragmatic. And as we've seen some of these studies come to completion and unblind, and look, we're finding that the implementation challenges are real and that the intervention may not have had as much uptaker has maybe not as much adherence or fidelity as one had hoped when planning the study.

And I'm wondering your thoughts about whether in doing these pragmatic trials, might we need to figure out ways to monitor more in real time, either fidelity or adherence, and would there be any time points that we might want to intervene so that we're sure we're still doing the experiment that we

thought we were trying to do from the beginning. And I'm curious, everyone's thought about those tensions on the explanatory to the pragmatic side, certainly from the funders perspective, we want to make sure the experiments being done. But how do we do that if we're relying more on these digital tools and other things, when we do pragmatic trials?

Lesley Curtis:

It's a really great question, Wendy, and a couple of things that come to mind for me, first of all, I think we absolutely have to figure out a way to do that. That is to actively monitor fidelity in real time, in terms of how, and when we do that, I think it depends, it will depend a lot on the actual trial that's being undertaken. I think the other thing though, that we can do as a community is really encourage people to be candid and share what is happening in their trials in real time. And that's something I would say that you and Kathy Myers at the NIH have really done throughout the Collaboratory. Which is encourage people to share what they're learning, what their challenges are with respect, to fidelity and adherence. So that we can learn where the stumbles are and then figure out how to advise people to advise them in the future. So I'll save the how and when for the others on the panel to comment on.

Patrick Heagerty:

Yeah, Wendy, I'll just add a couple of quick comments there. The role of a data and safety monitoring board is crucial because it's an external body that holds you accountable to the conduct of your trial. So having fidelity be part of that conduct evaluation, and having an external group to report to, I think is powerful. You ask a really hard question around when programmatic becomes variable, a broad range of participants and oftentimes a broad range of variations on a given intervention. How do we retain signal when we're introducing noise in both maybe the who and the, what that we're studying? I think it's a huge challenge. I think we have to be a little more thoughtful than about secondary analysis of big pragmatic trials and try and study some of those sources of variation.

Keith Marsolo:

And then the other thing that I would maybe add is, to the extent that then an intervention could be essentially deconstructed into various components, that might be a little more amenable to implementation in the EHR. So lots of EHRs have different ways of defining lists of patients for instance. And so rather than be specific around this big package that needs to be implemented, can you break it into different pieces that can then be tailored for the individual EHRs? And so it's more complicated as a design, but it may be a little more attractable and it may not work for all studies, but I think that that's one thing that can be considered as you go forward. Because in many cases, it's actually those sub components that are the most valuable, not the packaging and the construction around it. And so I think that that could be something else that people consider as they go forward.

Wendy Weber:

Yeah. I think it's a really important issue that we'll need to keep discussing as we look at these and as we learn as more and more of these trials get completed. What's worked and what hasn't, I think is something that we'll pay close attention to. Please join us for our next podcast as we continue to highlight fascinating and informative changes in the research world.

Adrian Hernandez:

Thanks for joining today's NIH Collaboratory Grand Rounds Podcast. Let us know what you think by rating this interview on our website. And we hope to see you again on our next Grand Rounds Fridays at 1:00 PM Eastern time.