Adrian Hernandez (00:04):

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.

Kevin (00:29):

Hi. Today we're here with Craig Lipset who will be reflecting on digital in trials, improving participation, and enabling novel endpoints. Welcome Craig.

Craig Lipset (00:38):

Thanks, Kevin. It's great to be with you.

Kevin (00:40):

Craig, do you want to just give a summary of the Grand Rounds that you did for us, which was so excellent?

Craig Lipset (00:45):

Thanks. Yeah, I'm happy to hit on some of those themes. I tried to break out some of the different uses of digital today in medicine development programs, in particular the way sponsors are looking at these today. And for me a lot of that has been grouping some of the use cases around either the ability to improve access to participation and access to information, or our ability to measure in new ways and exciting new endpoints or even traditional endpoints that we can measure in better and smarter ways, or our ability to automate and drive more efficient conduct of studies by automating different processes.

Craig Lipset (01:30):

But then during the conversation I tried to take a different perspective and look at these digital initiatives that are at times incremental and maybe just supportive to how we're running our studies today. And to contrast those to some of the digital use cases that actually may be more disruptive in terms of really changing things about how we're running our studies, changing elements like location. And then to be a bit provocative I reflected on some of the ways the trends in digital may actually displace some of the roles that we have in studies today. Could digital actually enable investigators, sponsors, or even patients to be displaced in terms of the roles that they have in research studies as we know them today? So those were some of the themes we hit on in the Grand Rounds together.

Kevin (02:25):

Great. Thanks. And as you said, one of the more provocative parts of your talk had to do with this idea of how digital is displacing different elements of the research enterprise. I was wondering, if can you go into a little bit more detail? And I know that you're in speculation mode but it was really interesting.

Craig Lipset (02:44):

Well that's the beauty of being in speculation mode. By having this recorded, I can pull it up again in 10 years if anything I said was even remotely accurate and if not, hopefully it'll just vanish on the internet.

Craig Lipset (02:57):

But there were three categories around displacing that I was sharing some thoughts on. And the first is, as we see these movements around how digital is democratizing access to many research grade tools and instruments and how that's enabling almost this do-it-yourself movement in research and development. I first started to get exposed to that from the work of Patients Like Me and how patients in that community were sharing data around the use of lithium and among ALS patients and their ability to almost drive what a patient driven research study could look like on their own without having the overhead of sponsors and investigators. But you're seeing that that spirit of DIY R and D all the way through to stories of the ability of DIY bio hackers using CRISPR on themselves or a story from last year of an individual who claimed he developed a therapy for his HIV and self administered it live on Facebook.

Craig Lipset (04:08):

Some of these are horrific but it does certainly point to this spirit of democratization and as better controls get into place, what does that mean for the traditional centralized research models as we've known them when these tools become much more accessible and in the hands of everyone?

Kevin (04:26):

Great. Can you say a little bit about the digital twin concept? Because I think that was something that captured people's imaginations.

Craig Lipset (04:34):

The concept of digital twins is interesting and a lot of it ... you can certainly find a lot written among manufacturing sectors. The idea of having a digital twin for a jet engine makes a lot of sense. It's hard to bring in the engine in and out all the time when there is different diagnostics to be run. But now when you look at the number of sensors that are embedded on just a single wing of a modern aircraft, these different components essentially have enabled this desired state of a digital twin of a machine that could be monitored centrally as if you were on site.

Craig Lipset (05:10):

And certainly as we look at the proliferation of electronic data about all of us as individuals, starting with health but then moving layer by layer into so much more data that is not only being generated but is being accessible to so many, it certainly creates an interesting opportunity but also some interesting concerns. It certainly is almost the intersection of precision medicine meeting the surveillance economy where we can be really excited from a data science perspective about the wealth of data about an individual to the point that we could almost emulate that individual without them needing to be there. Just based on the diversity of data we're able to access the sensor data that's feeding even more live.

Craig Lipset (05:59):

But then some of the concerns that may come up around some of those use cases. Certainly one that was raised on the Grand Rounds conversation was around synthetic control arms. And I think that this is a great example of how some of this data can be brought to bear in our ability to use contemporary data from other patients without the need to necessarily burden studies and burden research participants with one to one randomization between active and a control arm. But then there, I think, are very real questions and concerns when one's data starts to drift farther and farther away from their own self and

their own controls. One of the use cases for real world evidence that I think was very exciting from a regulatory science and a data science perspective right now has been being able to generate new labels for medicines based on real world evidence data, new populations based on how the data is being used in the real world. But even there a lot of the same questions I think are going to start to be raised.

Craig Lipset (07:08):

What happens when patients aren't aware of how their own data is being used? What happens when it's being used to support research that maybe they don't support? How far can my data, my digital twin, start to travel out of my own purview and control without requiring my consent and permission for use? And the richer and richer those digital twin data sets get, the farther and farther I think consumers will get from believing that this can truly be de-identified.

Kevin (07:40):

Oh, that's great. Thank you so much. One of the other things that was so interesting about your presentation was the discussion of the barriers that exist for meaningful adoption of digital technologies in clinical research. And I wonder as you think about the different stakeholders and players who are involved, what are some opportunities that some of those stakeholders have to address these barriers and make advances? What are some of the highest impact areas as you see it?

Craig Lipset (08:12):

There's so many great uses for digital today and some of them are certainly harder to adopt than others. There are some that can be very operational. There are some that can be very accessible for teams to be able to partner and use today to improve the design and the planning and the execution of a study. Some may be able to facilitate some elements of data flow, some may be able to improve the experience of patients in the study. I think those that start to engage around the actual data acquisition in the study, a new endpoint, a new way of extracting structured data from free text in an EHR, anytime we're starting to dabble with the technologies that are going to affect the data itself certainly raises a bar of complexity and make some of those use cases require a little more planning, a little more of validation and a lot more effort.

Craig Lipset (09:13):

So I think for a lot of organizations the opportunity to partner around some of the operating elements of the study in terms of its conduct, design and planning, those may be a little more accessible. But we certainly can't wait to do the planning that's required, the validation that's required together in terms of the real desired state with many of the new endpoints that could be a truly disruptive to how we're running our studies.

Kevin (09:39):

Great. Well, Craig, I want to thank you so much for sharing your thinking with us on these important issues today and it's been very stimulating.

Craig Lipset (09:48):

Thank you, Kevin. I appreciate the work of the group and the opportunity to share it.

Kevin (09:53):

So please join us for our next podcast as we continue to highlight fascinating and informative changes in the research world.

Adrian Hernandez (10:04):

Thanks for joining today's [inaudible 00:10:05] 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.