

Podcast 6: IMPACT-Afib: A Randomized Trial Using the Sentinel Initiative Platform

- Adrian H.: [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](https://rethinkingclinicaltrials.org). Thanks for joining.
- Adrian H.: [00:30] Hi there, welcome to today's podcast from the NIH Collaboratory. We want to welcome everyone. We just finished up a great Ground Rounds and today we're here with Rich Platt and Chris Granger who will be reflecting on IMPACT-Afib, an 80,000-person randomized trial using the Sentinel Initiative as a platform. So welcome Rich and Chris. I wonder at the beginning here if one of you could just give us a very brief overview of what you're doing.
- Chris: [01:01] Maybe Adrian I could start by just stating something that's an important background. That is, this is an enormous public health issue, the fact that atrial fibrillation is one of the most common causes of preventable stroke and that two thirds or more of those strokes could be prevented. And yet we've seen, including in the Sentinel common data query that only about half of patients are being treated, maybe even less than that, who have atrial fibrillation and risk factors for stroke and have clear guideline indications for this treatment. So we felt to begin with we had a compelling clinical gap that could be addressed with this type of a program. And then we had this concept that's based on some other work that we've done that if we have an education intervention focused on patients, that that might well help to close that gap with a low-level intervention, and that's critically important.
- Chris: [02:00] So the intervention that we're studying is targeting patients who have atrial fibrillation and are not being treated with anti-coagulants based on the information from the five data partners that are collaborating from the Sentinel collaboration, and identifying patients in these health plans that are candidates for the study. And then they're being randomized to either the patient education intervention, combined with notifying the providers as well, either an early intervention or a delayed intervention, in which case simply the provider is being notified a year later.
- Adrian H.: [02:40] Rich, tell me a little bit why Sentinel is a great platform for this? Originally Sentinel was designed for essentially safety surveillance. I find it very interesting that the FDA has taken on this of thinking about how can a pragmatic trial be used?
- Rich: [02:59] From the very outset Adrian, FDA has said that it wants Sentinel's resources to be a national resource for a wide array of activities. Particularly with the growing interest in using real world evidence, FDA saw an opportunity to test Sentinel's ability to serve as a platform for clinical trials. Among the things that's sort of a first here is our working across several health plans simultaneously. Health plans have done randomized trials before. In fact, essentially all of the Sentinel data partners had experience doing clinical trials. But the notion of coordinating across several of the nation's largest insurers by being able to use the Sentinel infrastructure was really new, and that was a major piece of what FDA was interested in testing. The goal here is to see whether this

intervention can actually improve the use of oral anticoagulants and improve health outcomes. But equally, to see whether it's possible for this to be a model for additional studies.

Adrian H.: [04:17] Now it's of note that this is a randomized trial. Chris, I wanted you to comment, is that the normal process it seems like for health plans or health systems would just be to, if they do anything, to just send a letter out to say, "You have this problem and you should consider X." Why is randomization important here?

Chris: [04:40] Well Adrian, we were really fortunate to have the group that we're working with, the leaders of the research arms of each of the health plans working with us. They were very eager to have a rigorous design because it's very uncertain, whether or not these mailings, these communications to their patients, are making an impact on their care and their outcome. So there was a desire to have a rigorous design, and the opportunity to randomize patients is the most rigorous design with the most valid control group in this project.

Adrian H.: [05:19] Rich, I wanted you to comment a little bit about the sample size here. It looks like it's an all-in approach, which is not the typical way we consider sample sizes. How did you guys decide that?

Rich: [05:33] In these health plans that meant, among people who would be eligible for intervention because of the contractual relationships that the health plans have with the purchasers, that meant looking for everybody who was eligible. Our headline title for the webinar we just had was An 80,000-Person Randomized Trial. At the end of the day it'll be closer to 88,000.

Adrian H.: [06:02] Do you guys have any sense of, what's the expenses that health plans or health systems are enduring just sending out information? Chris, you commented earlier that some of these health plans are sending out information about health problems but no one knows whether that is effective.

Chris: [06:23] Well it's commonly done Adrian, as we know, including to providers as well as to patients, to send information. And as is true of all too many things we do in healthcare, the confidence that that's making any real difference is low. We simply don't know what the impact is of much of this activity. The individual cost of mailing a information sheet or communication to a patient is modest, but the cost of sending it out to thousands or tens of thousands or hundreds of thousands of participants in these health plans then becomes substantial. So I think there is a real desire to know, is this type of activity having an effect?

Adrian H.: [07:10] So Rich, I wonder if you could get a sense on the cost here for doing the study.

Rich: [07:18] It's an order of magnitude improvement over the usual cost of interventions, but it's not close to being free.

Chris: [07:27] But Adrian, I will point out, those of us who have been more accustomed to the cost of a traditional randomized trial, especially when we're talking about including important clinical outcomes as part of our objective, is hundreds of times the cost of what we're talking about here. And as you earlier pointed out, we're also taking an approach where we're including all eligible patients, because we have constructed it such that it fulfills the criteria for waiver of consent. So we have a study that's both more efficient and more generalizable.

Adrian H.: [08:09] So Chris and Rich, thanks again for a great podcast. I really enjoyed hearing about IMPACT and what we'll see down the road, leveraging Sentinel for our pragmatic trials. As a reminder, our next podcast will be with Andrew Faucett on Considerations for the Return of Genomic Results and will be posted the week of February 12th. Thanks again for joining us.

Adrian H.: [08:33] Thanks again 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 p.m. Eastern Time.