Jill Harrison: Hi, this is Jill Harrison, executive director of the National Institute on Aging Impact Collaboratory at Brown University. Welcome to the Impact Collaboratory Grand Rounds podcast. We're here to give you some extra time with our speakers and ask them the interesting questions that 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 the companion grand rounds content can be found at impactcollaboratory.org. Thanks for joining.

Vince Moore: Good afternoon, everyone. This is Vince Moore. I'm one of the principal investigators of the Impact Collaboratory NIA funded grant, which is focusing on identifying then funding and supporting and monitoring the activities of pilot projects that are designed to take ideas that work when researchers do them to and then embed them into healthcare systems in a pragmatic way to try to get new ideas and new programs so that they're available to improve the quality of lives of people living with dementia and their caregivers.

And today we have with us, Dr. Scott Halpern, who's professor at University of Pennsylvania and runs a large program where he sort of does the epitome of what we're trying to do, is runs pragmatic trials and he just gave a stellar grand rounds focusing on the summary of his history doing pragmatic trials and struggling and grappling with various scientific and application challenges in that process. Scott, I wonder if you would just sort of give us a brief summary of the going from that first trial you did, which cost a $158 per case or $258 per case to the ones you did costing $20 a case and what are the ideas and great insights you had from that?

Scott Halpern: Yeah. Well, thanks Vince. Yeah, the numbers are even more stark. That first trial, I think we estimated cost more than $1,500 per patient enrolled and we got about four of them each month into our trial. It was half my career's worth of work for a 140 patients or something. And it just really struck me that for a lot of the work that traditional translational researchers do where they're trying to bring a new drug or a new physiologic intervention to the marketplace, one really needs to take a highly meticulous, constrained approach to ensuring homogeneity in the patients enrolled and clear removal of any contaminating factors in all of types of procedures one would put in place, when the goal is truly to delineate efficacy of an intervention in a very controlled, highly regulated fashion. But then a lot of the work that we're really interested in doing, which are more behavioral interventions and learning to do things within the context of large health systems, not only doesn't need those things, but is much better suited without them.

And so now we take approaches to our areas of interests that are intrinsically scalable if they're successful. We almost don't do anything that can't be immediately directly scaled if we show overall real world benefits. And yeah, instead of 1,500 bucks a patient, which actually by NIH standards is still not a bad deal. We're now down to, in the 50 buck or so range and getting hundreds, if not thousands of patients enrolled per month. And I didn't even have chance

to talk about all the complimentary studies in areas outside of serious illness that either my team or my colleagues' teams are doing here at Penn, but in areas like promoting driving safety and technologic approaches to increase remote monitoring in COVID and lots of other cases, but having similar economies of scale in their very pragmatic efforts.

Vince Moore: Great. One of the points you made in your lecture, which thinking about it awful lot is the sort of phase three trials, the explanatory trials, the ones that cost so much money where researchers really need to understand in some sense, what the mechanisms are under that. That then translates out to these more pragmatic things embedded in healthcare systems, which are going to scale. We've had this conversation that it's not just that only in phase three trials that can you actually begin to understand something about the mechanisms, the issues, about how to actually get to implement and do the implementation work around that, but that you can also try to do that under pragmatic structures. Can you give us an example of how you've done that in your work?

Scott Halpern: I think lots of times real mechanistic insights can be derived through pragmatic trials and oftentimes it's augmented, the goal of doing so, is augmented by pre-specifying how the effects of the interventions differ in high fidelity settings versus low fidelity settings, can help understand the likelihood that there's truly a causal relationship and hence yield true insights.

Vince Moore: That's the wonder of implementation science and I'm learning more and more about that as we move on. In the lecture, you talked a little bit about this concept of accountable justification as a way of getting people to sort of sign off and say why they didn't want to refer someone for instance, for palliative care otherwise. What is the theoretical background of this accountable justification? And is it really because sort of people are just being lazy? Or is it they want to avoid being lazy? Or they want to be avoid? What is the action that's being taken here?

Scott Halpern: It's a great question. And actually, I think there are so many different aspects for why accountable justification can work and the operating features or the operative features may be different in different context. This may in fact be one way in which the actual mechanism is not perfectly elucidated, but at the end of the day if it works, it works. What are the many potential ways in which accountable justification works? Just to review, for those who don't use the term all that often, the idea behind accountable justification is you ask people, have they done the thing that you are trying to get them to do? And if they say they've done it, you take them at their word and if they say they haven't, then you ask them to just explain why.

And what we know about accountable justification is that the way in which you ask them to explain why and where that information becomes available goes a long way towards determining how effective the intervention is. For example, if you give them a list of dropdown menu items to select from as to their reasons

for not doing it, it's not going to work quite as well as if you force them to enter in a free text box, their actual reasons for not doing it. And why might that be? Well, it's too easy to just select from among a menu of options and if you make the task a little bit harder than people might say, "Hmm, maybe I should just do this. It's obviously a strong recommendation."

The other is that without leading people to think that there are justifiable reasons that you would include in that dropdown menu, that you're maybe making them second guess whether their reasons are actually legitimate. But I think among the most important parts of accountable justification in terms of why it really works, particularly as a way to nudge clinicians, is that clinicians don't like to be put in the position where they don't feel like they've got a clear way to justify on rational grounds why they're doing X or not doing Y. And just forcing them to think about it and come up with a good reason and showing them that if they don't have a good reason, it's going to be available for others to see in an electronic health record is itself pretty motivating for an otherwise competitive crew of intellectual people.

Vince Moore: Great response. I would like next ask you about to comment on the sort of, it's not a duality, but it's a continuum of the nature of sort of these kinds of interventions that we embed in healthcare systems. Some can be very complex, which have multiple individuals sort of having to coordinate and you then achieve some goal and then have to improve in some way. And they're like care coordination or care planning or something like that. These are complex kinds of things where you have to sort of train people to behave in a slightly different way and to take things into consideration. As distinct from things that are sort of more light touch, more of a nudge, more of just simply altering the decision frame as in accountable justification. What context does a heavy touch or a high touch work as opposed to a light touch being sufficient, in general you think?

Scott Halpern: Well, I guess I would say two things about that. One is that it's not always an either or situation. Sometimes in a lot of the work we're doing, uses light touch interventions, for example, nudges delivered to clinicians through the electronic health record, to motivate high touch behaviors, such as real integrated palliative care, goals of care discussions, things of that nature. Sometimes the one gets combined with the other. But certainly I think there is an important distinction to be drawn between the complexity and resource intensiveness of an intervention and how quickly one ought to progress through the sort of NIH stages of behavior change research. If you take a light touch intervention that we know works in many other settings, like just changing from an opt-in to an opt-out, that's sort of shovel-ready to be tested in a large pragmatic design, because if it doesn't work, you find it out quickly and you've really lost very little.

You haven't spent a lot of resources thinking about exactly how one generates the perfect intervention before you get to large scale pragmatic testing. On the other hand, if you're coming up with a new, highly resource intensive, high

touch, human dependent intervention, you better be pretty sure you've got some compelling efficacy data to support it before you go ahead to a phase four or phase five trial in a large scalable setting, because there, if you're testing the wrong intervention, you've spent a lot of money and a lot of time and a lot of people's bandwidth to get a null result. I think that's really a key difference. And I know many people at NIA and elsewhere throughout NIH kind of share that view that the nature of the intervention goes a long way towards determining whether it's ready to go to pragmatic testing or not.

Vince Moore: That's great. Great response. Thank you. Last, long time ago, I was on the scientific advisory board for the SUPPORT trial, which was one of the first large, large trials to look at serious illness care in the hospital setting and their intervention was essentially trying to give feedback to physicians about the probability of their patients dying within the next six months, and then a nurse advocate to help with other kinds of things. And I'd like you to sort of contrast that idea, which at the time, they didn't have the great technology or EMR, et cetera that we have in these days, with what you're currently planning on this PONDER trial, which I was very interested in hearing about.

Scott Halpern: Yeah, well, so the SUPPORT trial, which I believe had a budget in the $28 million range by early 1990's dollars. I'm not an economist, so I don't know how much inflation there's been since then, but it's a lot of money. That was an entirely negative trial. And I think there are a number of reasons for it. The first I would say, and I'll explain why I think that study was negative as a way of contrasting with what we're hoping to do. That was a trial of information provision at its core. They provided clinicians with information about predicted mortality within six months. They provided clinicians with information about what they knew about the patient's goals and preferences and then kind of left them to do what they will with that information.

There's a classic schematic that was produced back in 2006 or 2007 by the Nuffield Council in the UK, which is a public health advisory council that talks about the intervention ladder of behavior change. And on the bottom are things that don't work very well, but no one gets too bothered by it and on the top is things that work really well, but might lead at least some libertarian folks to have a little agita. And the information provision is unambiguously at the lowest rung of that ladder. Sure, who's going to argue with giving clinicians information? But arguably you find a problem in clinical medicine and the root cause of that problem typically is not lack of information. Information provision is about the weakest possible way to change clinician behavior imaginable. I think that's one reason why SUPPORT didn't work.

The other reason is that in some ways it was ahead of its time to be able to work. This was done in an era where there was very little inpatient palliative care, let alone longitudinal models of care that could help people once they got out of the hospital. In many ways, SUPPORT failed because it was conducted in an era that didn't have the requisite infrastructure to support success. It just

couldn't happen because it was a narrow intervention in a complex problem without the underlying infrastructure to support those patients, even if their goals were to be respected.

By stark contrast I think, what we're doing is trying to tap into the heuristics and cognitive biases that pervade clinical decision making because clinicians are first and foremost humans and so they have these same heuristics and cognitive biases that all other humans do. And by tapping into those innate cognitive processes, that's a much stronger way of intervening than just providing information. As counterintuitive as this might sound, telling a doc what a patient's prognosis is, is very likely to be less effective than asking the doc to think about the patient's prognosis or forcing them to think about the patient's prognosis because otherwise you're just basically making it too easy and that's not going to help the doc see the forest for the trees if you just give them information. He'd be like, "Oh yeah, tell me something I don't know. I got it. Yes. Patient's very sick. Already noted, thank you."

But if you force a doc to actually take the time to think, if someone really forced me to predict whether this patient would be alive or dead in six months and if I think they're going to be alive, what's their quality of life going to look like? What's their functional status going to be? That's a much more cognitively engaging intervention that at least we hypothesize will be much more likely to change behavior.

Vince Moore: Great. I'm so glad I asked you that question because you actually elucidated very nicely, basically 30 years of research and changes in how people are thinking about these interventions. Dr. Halpern, thank you so very much. It was a tour de force lecture and great response. Wonderful time talking to you. Thank you very much for your time.

Speaker 4: My pleasure and thanks for the invitation again, Vince,

Jill Harrison: Thank you for listening to today's Impact Collaboratory Grand Rounds podcast. Please be on the lookout for our next grand rounds and podcast next month.