Jill Harrison: Hi. This is Jill Harrison, Executive Director of the National Institute on Aging IMPACT Laboratory 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.

Susan Mitchell: Hi, Vince.

Vince Mor: Hi, Susan. What a pleasure to see you.

Susan Mitchell: This is very fun to be interviewing you on your Grand Rounds. We're talking all about implementation and the challenges and boy, your talk really highlighted some of the challenges of implementation and embedded pragmatic trials, just like in the real world. I'm going to pick up on a question that was in the Q&A that we didn't get to, and really it relates to the fact that there's certain practices or units within practices, like nursing homes and a healthcare system, may be very good at implementing new programs and others not so good. We sometimes talk about a third, a third, and a third.

Susan Mitchell: The person asked a question. She said, "How or should you actually try to identify 'best places' a priori in selecting your sites, or does that really undermine the pragmatic intent of a trial?"

Vince Mor: If I understood the question correctly. It's not should you pick the best sites. It's actually can you sort of design a way to predict who's going to be successfully implementing and who's going to be less successfully implementing. The perfect design is if you had such an instrument to be able to, say you pick up 50 or 100 nursing homes or hospitals or physician practices, and then had some way of predicting which ones of them are going to be more engaged and which ones will less engaged in the intervention as you move forward. Whatever that might be.

Vince Mor: Then you could actually incorporate that into your random assignment. You could actually stratify based on the third, a third, a third based on this instrument. Then you could actually do analysis based on the third that did it and the ones that were in that strata who are the controls who were not exposed.

Vince Mor: Of course, the same thing you could do by in that stratified approach and then you would hopefully, if your prediction were accurate, even if it weren't hugely accurate, you'd still get an enormous amount of extra boost from the study design where you could a priori stratify places based on the degree to which they will likely have fidelity and implementation of the intervention. Because otherwise, if you don't do that, and you only have the measurement of the fidelity in the experimental group, if you don't know who in the control group

would have been in that pool of high utilizers. You can do some post hoc stratification and then say, "These are the controls who look like they would have been like the experimentals that did it."

Vince Mor: In our proven study, we haven't yet published this, but we do have analyses that was done by our statistician, Roee Gutman, and his graduate student that use this post hoc approach basically through a matching mechanism. There, we did see that those controls that looked like the experimentals that did a lot of implementation, there was a statistically significant effect on the primary outcome of hospital transfers avoided. But that's kind of like that you're doing a matching so it's no longer a random assignment trial.

Susan Mitchell: Okay. Devil's advocate though. If you know ahead of time, some way to predict the worst implementers, why even bother with them?

Vince Mor: That's a great question, which actually gets me to another point. Ultimately, these embedded pragmatic trials are supposed to inform the stakeholders who will decide whether or not to implement this intervention as a standard practice throughout the entire healthcare system. I'm going to now give you an example outside of the domain of dementia and think about this. This was a study that was done by Susan Wong as part of the NIH collaboratory study, where they were looking at Hospital Corporation of America hospitals, and they were doing universal bathing with a particular kind of soap product on a daily basis to reduce the likelihood of infections. Now, they actually had fairly high levels of implementation. It was variable, but fairly high levels of implementation in all of the experimental hospitals. They had much more intense monitoring in both the experimental control hospitals. At the end, their primary outcome of basically infections for all people who were bathed, regardless of all comers, that did not achieve statistical significance in their outcome.

Vince Mor: Their primary outcome was not "statistically significant", but a secondary outcome of those people who had the highest risk of having an infection, that is those people who had some form of implanted device or some kind of catheter or something like that, that they had. Those people who were bathed, there was a very statistically significant reduction in the infection rate. The company of Hospital Corporation of America actually got those results and said, "Okay, we can actually identify a particular focus, implement this whole heartedly throughout the entire system and recognize that it could be difficult to implement." They actually gave their hospitals a choice to sort of do it for everybody because there was no harm and it reduced the complexity of the way in which orders were done, or they could do it just for those people who had devices or other kinds of complications.

Vince Mor: Similarly, if proven, if we didn't know which nursing homes would have not been doing the implementation very well, then the company would not have known that the effect they were getting was largely concentrated in nursing homes that were actually doing the intervention. If they could sit back and say, "All

right, this intervention of video, minor complications, and I get more or less half of my places to do it a little bit. The third do it a lot. And I'm happy because I'm reducing a little bit by 1%, or even a percentage and a half, all hospital transfers of patients." Because for the work they're now doing, because they're an accountable care organization, they lose money for every hospital transfer because they are on the hook, like an HMO for the whole thing.

Vince Mor: From their vantage point, it may not even matter that the bottom half is not doing it very much because the top half is doing it and still saving them money, even though it's not statistically significant. Without having all of the information, they may not make that decision. It absolutely happens that in a bunch of their nursing homes that are still part of accountable care organizations in Genesis or one of the companies that was involved with us, they're still using those tablets.

Susan Mitchell: Interesting. I'd also one thing occurred to me as you were talking that if you a priori discount or make ineligible your worst performing facilities, you do sort of perpetuate healthcare inequities because you're not allowing the worst performers, the poorer quality to better themselves. There's a problem with it.

Vince Mor: You're absolutely correct.Not only that, it's not just you're doing it in the trial, you're actually structurally doing it in the dissemination phase because the company's going to ignore those poor performing places. Whereas if you give them tools and information, say these poor performing places would be better if you could do more in that world or somehow or another, give them an incentive to do so. Particularly if they're part of an accountable care organization and they have some incentive money to actually make that possible because they could benefit and they could do something in this area. For more complicated interventions that are ultimately more costly, then it's a more complicated calculus. But it's a more complicated calculus for the entire system.

Susan Mitchell: Let's turn a little bit more focused on ePCTs and dementia. Dementia is a complicated disease with complicated health services, delivery issues, and juxtaposed to this issue where it seems to be the more complex interventions are clearly the more difficult ones to ensure adequate implementation, suggesting that maybe we should just do nudge trials or simple interventions. How do we reconcile that with the fact that the solutions for people living with dementia are probably not going to be solved with a nudge or a simple intervention?

Vince Mor: One, I'm not sure we actually know that. I'm increasingly thinking of things on two continuum. One is the one I talked about in the study, that is the continuum of complexity. You have a simple substitution and then a much more complicated thing like interact, which is we've got to do all this training and all his other restructuring of the way work is done by nurses in a nursing home, for example. Then the other continuum is actually the light touch versus a much

more complex touch. It's not clear that simple substitution is always a light touch. It's a light touch could be much more like a nudge and what we don't know is, as you look at that two dimensional array is what's the relationship? What do we know about the different kinds of interventions that might be efficacious? Let's say, in a nursing home setting or in a doctor's office. What do we know about the efficaciousness and their effectiveness in that sort of two by two space?

Vince Mor: We just don't know the answer yet. We haven't assembled the data yet. It's also the case that some things that appear to be complicated when they're done in an efficacious intervention, a caregiver support group with all this other kind of identification of the caregiver and so on and so forth, where we're actually trying to intervene with a population. You might be able to do that in a much simpler way in a centralized strategy. For example, if you're forget nursing homes for a moment - you're a Medicare advantage plan and you're trying to support caregivers or care partners who are having difficulties with managing their caregiving role with their demented patients who happened to be members of the Medicare advantage plan. If you could find a way to reach out to those care partners or so on and so forth, you could actually think about them being called or making a call to an 800 number or to this, and then to actually recruit them.

Vince Mor: In that sense, you are reaching the people who are at their wit's ends because in fact, they're volunteering to be part of it. Then you actually still do the analysis of whether or not this happens over the full, this is effective over the full population. Let's imagine you have 10,000 experimentals and 10,000 controls where Medicare advantage, who all meet some criteria for some level of dementia. Maybe it's 5,000 and 5,000. Doesn't really matter. Then you reach out to them, try to stimulate them. You give them multiple reminders or text messages or what have you. Or very nice letters, et cetera. Then let's say 25% of the care partners actually sign on and click and have a phone call. Then some of them actually then join a virtual support group of some sort. What you're doing is you've got, let's say one fifth of the people who are getting the full dose, but they're the people who are maybe who need it most so they're getting it.

Vince Mor: Your analysis, you don't know who those are on the control side. You might be able to come up with some a priori stratification or just post-hoc, but you ultimately are going to be doing your analysis. What difference does this make to the bottom line for the MA plan or for some other measure. The level of frustration of their primary care doctors or what have you. It's still you're able to do that and that is not a light touch intervention, but it's a more targeted intervention that requires the behavior of the subjects in terms of their election.

Susan Mitchell: Sounds complicated.

Vince Mor: It is, but it's much simpler than training somebody in every doctor's office.

Susan Mitchell: I see. So you're talking about ... I see what you're saying about a nudge, a behavioral nudge, to do something on the part of the recipient really.

Vince Mor: It could be reinforced by the doctor. It depends on how good your system is.

Susan Mitchell: That's a little bit like what the Bluestone is turning into, where we're sending information to the family, nudging them, the advanced care planning, but not relying on the providers to reach out to them.

Vince Mor: Right. You sensitize the providers by doing the training. The alternative might be to actually, when the providers come in, let's say in the doctor's office, that the EMR has some pop-up reminder that doctor said, " Hey did you reach out for this? Did you do that?" Because there's a reminder during the course of the visit or what have you, or the nurse, or somebody could do that. Now, in the Bluestone case, because those nurse practitioners and doctors don't have any support people, it's more complicated.

Susan Mitchell: We've talked a lot about implementation and, to me, we've talked about this before. There's two real points where these pragmatic trials can go awry. One is the implementation, as we've discussed. The second is the outcome choice and measurement because it seems to me in pragmatic trials, we sometimes have to rely on a more distal outcome that is measurable using secondary data sets, but may either be very hard to move the needle or not exactly what we want in terms of measuring the effect of an intervention. I just want you to comment on that, on the other side of the equation of the challenges. Not just of implementation, but measuring. Even if there was a 100% uptake of the intervention, the challenges of the outcome, measurement.

Vince Mor: Caregiver support. Let's just imagine that. It's most people when they're doing efficacy trials, phase three trials, they go in and measure people's satisfaction or their frustration levels or their quality of life in some way or stress or things like that. When you think about that in a pragmatic sense, you say, "Well, in a distal way, there's that more proximate thing of what the stress level is and you could measure that way if you actually spend the money to do that." Another measure is are people prescribed an antianxiety agent or do people like most distally get to the, patients go to the nursing home or have multiple ED visits because of something or other. Those are distal outcomes, which are going to be much less, much more rare. It's a more difficult thing to move the needle.

Vince Mor: You have a much bigger sample size and that means a much bigger study. That's the problem is that the relationship between the proximate outcomes that people care about, the caregivers care about, and the distal outcomes that the healthcare system might care about because it relates to money or the frustration of the doctors and other kinds of things that are complicating the healthcare system. Those may be very tenuous relationships.

Vince Mor: I think we need to be much more creative about how we figure out how to do this with better engagement of people, better approaches to getting both experimentals and controls, intervention A versus intervention B, to actually participate in some kind of web-based survey that the patients would actually do or you'd measure the outcome that way. You'd have a distal outcome in the more proximate one, which might be a little more biased, but it's still not going to require primary data collection outreach and so on and so forth. It requires someone to answer a short sort of web-based call that has other implications in terms of who's able to do that and who's not able to do that. You can do it through the phone, not phone, but those are the challenges. I don't think we should say you can't do it. I think we just have to be more creative about how we do it.

Susan Mitchell: That seems like a good place to end. We're learning a lot and hopefully moving this methodology forward with our experience. Thank you very much.

Vince Mor: My pleasure. I enjoyed it.

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.