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.

Jill Harrison: Hello everyone. I'm Jill Harrison, one of the executive directors at the NIA IMPACT Collaboratory. I'm joined today by Claire Chan. Claire, thank you so much for joining me today.

Claire Chan: Thanks very much, Jill.

Jill Harrison: As you know, the NIA Collaboratory hosts a monthly grand rounds series each with a companion podcast. And this past week, you presented a grand rounds that was extremely well attended around pilot and feasibility studies for pragmatic cluster randomized trials. Today, we're going to dig deeper into some of the questions that we did not have time to answer during the grand rounds presentation. So Claire, again, welcome.

Claire Chan: Thanks very much, Jill.

Jill Harrison: Let's dig right into some of the questions that lingered after your grand rounds talk. Can you elaborate on some of the hallmark characteristics of pilot and feasibility studies? Please just remind us, how are they defined and how would we know one when we see it?

Claire Chan: Sure. So, the two main ways to recognize a pilot or feasibility study is that they have a forward focus and their primary objective is feasibility. So, a pilot or feasibility study is in preparation for some future study or a future stage, and the focus is on ascertaining the feasibility of proceeding to that next stage. And we can see this from the definitions that feasibility studies are studies that ask whether something can be done, whether we should proceed with it, and if so, how? While pilot studies ask the same question, but have a specific design feature. And that's in a pilot study, a future study, or part of a future study is conducted on a smaller scale. So given their forward focus and their focus on feasibility, other hallmark characteristics we might expect to see include progression criteria, which are the criteria to guide the decision of whether to proceed or not to the next stage.

Claire Chan: And this might be in the form of formal thresholds, perhaps following the traffic light system recommended by Avery and colleagues of Green, where the criteria are met and the study can proceed, and where some changes should be made before proceeding, or red indicating it's inappropriate to proceed. Or the progression criteria be in the form of guidelines rather than formal thresholds, particularly where qualitative work is involved and an independent trial steering

committee might be involved in guiding the decision process. Some other hallmark characteristics we might expect to see include a sample size rationale based on the primary feasibility objective. So, typically, pilot and feasibility studies are small, but this wouldn't be the way to recognize a pilot or feasibility study.

Claire Chan: And, as mentioned during my talk, we see a lot of studies that are small, underpowered studies claiming to be a pilot or feasibility study when in fact they're a trial with a primary outcome of effectiveness that should be properly recognized as a main trial and powered and reported appropriately. So the primary focus of the pilot or feasibility study is feasibility. And so the sample size rationale should be appropriate to answer this primary feasibility objective.

Claire Chan: Another hallmark characteristic we might expect to see includes analysis that is mainly descriptive with a focus on confidence intervals rather than P values. There shouldn't be hypothesis testing for effectiveness and methods should be specified for how each of the pilot or feasibility study objectives will be addressed, whether qualitative or quantitative. Missing data would be explored rather than dealt with in a pilot or feasibility study. In particular, looking at the extent of missing data, understanding why data are missing, and investigating what can be done to prevent missing data in the future study. So, these are the main things to look out for in order to recognize a pilot or feasibility study when we see one. A primary objective of feasibility, a forward focus with progression criteria, and sample size, rationale, and analysis to match the primary objective of feasibility.

Jill Harrison: Thank you so much for that explanation. So clear and really helps to operationalize one of the vexing problems that the field is facing in terms of defining pilot and feasibility studies and clearly delineating the boundaries, and you've done a great job of that. You know, one thing that really piqued the interest of our listeners during the grand rounds was this idea that pilot studies and feasibility studies are related in that pilot studies are subsets of feasibility studies. Could you describe that phenomenon a bit more?

Claire Chan: Sure. So yeah, this comes from the definitions. So initially when we set out on our research to define pilot and feasibility studies several years ago, we'd planned to come up with a single definition for pilot and feasibility studies. But as we progressed in our work and conducted a Delphi survey, the results of this indicated that we needed two separate definitions. And yet at the same time, the definitions needed to be linked. So, we developed the definitions mentioned already. So, feasibility studies ask whether something can be done, whether we should proceed with it, and if so, how? And pilot studies ask the same question, so they're linked, but has a specific design feature in that, in a pilot study, a future study or part of the future study is conducted on a smaller scale.

Claire Chan: And the corollary of how these are defined is, as you mentioned, that pilot studies are a subset of feasibility studies. So, if we were to explain this a bit

more, if we were to draw a diagram, we might draw a large circle that contains all feasibility studies. And then within that circle, we would draw another smaller circle and that would contain pilot studies. And from the diagram, we would be able to see that all pilot studies are feasibility studies, but not all feasibility studies are pilot studies. So, this is what I mean about pilot studies as subsets of feasibility studies. The two have different definitions but are also connected.

Jill Harrison: Thank you for that. And one question that we did not get to in our grand rounds earlier this week is from one of the principal investigators of the IMPACT Collaboratory, Susan Mitchell. And her question was around pilot embedded pragmatic clinical trials. And specifically, what's your opinion on how much adaptation of an intervention is acceptable? For example, someone wants an investigator that wants to adapt an efficacious intervention for a Latino population. How much adaptation of the intervention is acceptable before they need to go back to an earlier stage of intervention development?

Claire Chan: Thanks, Jill. So this is an interesting question. So in terms of when it's necessary to go back to an earlier stage of the intervention development, we can think of it in two categories, I think. So, when the intervention has changed and when the population has changed. So, if the intervention hasn't changed at all and we simply want to see whether it would still be effective in a different population, then this is a question of whether we can generalize the findings from our effectiveness trial, in one population to another. And if we're not sure, then it might be appropriate to conduct another pragmatic effectiveness trial in this different population. And in terms of whether it would be appropriate to go back and conduct another pilot or feasibility study, we need to ask ourselves the question of whether we have any uncertainty about feasibility of this new trial.

Claire Chan: And we can think through the 10 domains that I described in my talk. So, for example, would the intervention be acceptable to stakeholders and used in clinical practice in the new population? You might no longer be certain about this because the stakeholders and clinical practice have changed. Is the research ethics approval process feasible? Again, this might be different in a different country and population. Does the proposed method of identifying participants correctly identify eligible participants? And the proposed method may have worked in the previous population, but are we still certain it would work in the new population? Can we successfully recruit participants that resemble the new population that would receive the intervention if rolled out? Can we successfully recruit a variety of sites that resemble the new settings where the intervention would be used? And we can think of other questions going through the rest of the domains in a similar way.

Claire Chan: So, that's if the population has changed. If the intervention has changed, then you ask how much adaptation of the intervention is acceptable before needing to go back to an earlier stage. I think if the intervention's changed substantially, then it's almost certain that one would need to go back to an earlier stage. How

much the intervention needs to change before we go back depends on the specific context. And as with when the population changes, if the intervention changes we need to ask ourselves again the question of whether we now have some uncertainty about feasibility.

Claire Chan: And again, we can think through the 10 domains I described in my talk. So if I go through a few, for example, would the new intervention be acceptable to stakeholders and used in clinical practice? Can we successfully recruit participants for this new intervention that resemble the population that would receive the intervention? Are staff willing and able to deliver the new intervention without additional training or support? Is some minimum level of adherence possible? And the key question to ask ourselves whenever we're trying to decide whether a pilot or feasibility study is needed is, do we have any areas of uncertainty? And this is the main question that should help guide our decision as to whether or not a pilot or feasibility study is needed and whether we need to go back to an earlier stage.

Jill Harrison: Thank you so much, Claire. I wonder if we could dig into this topic just a little further because we often hear of investigators struggling to identify and define track what the active ingredients of an intervention are that can be standardized across different sites as they embed their pragmatic trial across different healthcare settings, different organizations. Tips for that? Do you have tips for that? For understanding what the active ingredients are versus what are the adaptations that may be more fluid?

Claire Chan: Thanks, Jill. So, yeah, it's probably a tricky question to answer from a statistician viewpoint. It would definitely be one that the whole trial team would need to look up, especially the clinical side of defining exactly actually what it is about the intervention that makes the intervention. I mentioned in my talk about the importance of that particularly for a pragmatic trial because you're trying to find those elements of the intervention that really need to be delivered well and adhered to in order for the intervention to work at all and those parts of the intervention that can be flexible and allow for a more pragmatic nature of the trial. So, yeah, it's hard to define exactly which parts of the intervention would be the kind of core elements. I think that would be quite context specific for the specific trial that's involved. Sorry, hopefully that helps somewhat.

Jill Harrison: Mm-hmm (affirmative). It does. Thank you so much. Well, Claire Chan, thank you so much for your time and knowledge, really sharing so much about pilot and feasibility studies for pragmatic cluster randomized trials with the NIA IMPACT Collaboratory listeners. For listeners that are interested in learning more about Claire's work, you can find her at the The Institute of Population Health Sciences at Queen Mary University of London, as well as I direct you to check out the Pilot and Feasibility Studies Journal, of which Claire's the associate editor. Thank you so much, Claire.

Claire Chan: Thank you for having me.

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.