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.

Susan Mitchell: So good morning, Dr. Wilkins, I'm really glad we have another chance to talk further, but it's great to have you.

Consuelo H. Wilkins: It's great to be here.

Susan Mitchell: So fascinating Grand Rounds that you gave last week, and I have a lot of questions or input that I would love to get from you. So you probably know that the IMPACT Collaboratory's mission is really to build the nation's capacity to do embedded pragmatic trials in people living with dementia, in partnership with health care systems. And I really believe that if we don't figure out ways, practical ways, to embed health equity into the science of these trials at all levels, we're really going to fail at our overlying mission.

Consuelo H. Wilkins: Agreed.

Susan Mitchell: Yeah. And I think a lot of us have some idea now, a reasonable idea, and increasingly learning what health equity is, but the challenge is really how to address it, and I feel like some of this is developmental where stage one was learning about really what it is, and we really need to move on to stage two and to figure out how to do something about it. So our mission has three pillars, knowledge, generation, and dissemination, enabling and funding EPCTs or pragmatic trials, and the third is building investigator capacity. So I just wanted to talk about pillar one first and get your insights.

Susan Mitchell: So I want to bring up something I asked at Grand Rounds, and I want to go into it and see if I can push you a little bit on it. So we've been funding these pilot studies, and we've learned pretty early on that the pipeline of evidence supporting interventions for people living with dementia that are really ready for a pragmatic trial, in other words, they already have some level of efficacy evidence, are somewhat few and far between, and so already to move something like that to a pragmatic trial, there's a bunch of adaptations that need to happen, and we've gone on and on about whether these adaptations require going back to the first part of the stage model, or whether we can do them reasonably to prepare these trials for EPCTs beforehand.

Susan Mitchell: And so we are getting a few applications targeting minority populations, a few for particularly in Latino populations, and we might have a reasonable intervention that's been done more generally for dementia, and they want to modify it, the investigator, for a Latino population. We're also in a bit of a race

against time. So in Grand Rounds, you were pretty clear that you felt, even still we have to move back to stage one—I'm talking a lot, but I'm setting the scene—to do these adaptations. And I really want to push you on this because of the time element, in terms of adapting these interventions for minority, people of different background, do we really have to go back to stage one, or is there some shortcuts or some wiggle room there?

Consuelo H. Wilkins: No, I remember the question very well, and I remember being pretty definitive in my answer there. And that was purposeful, because we were towards the end of the time, and I wanted to make sure there was not too much ambiguity in my answer there. But it's certainly a lot more nuanced than "yes, you have to start over." It depends on what kind of intervention we're talking about, and how it was studied, and what elements of that intervention we actually think work, or are the reasons behind why these interventions work. So it certainly is a lot more complex than just they all have to restart, but the reason I was more definitive is because I think people see that as an opening to not critically evaluate the evidence, and thoughtfully consider whether or not this should work.

Consuelo H. Wilkins: So if we are talking about adaptations that are really related to culture and behavior and access, and those sorts of things, we should not presume that it's going to work in a different population of people that it's not been adequately tested in. So we make this mistake of assuming that we're now ready to test something that already has evidence that it is going to work, and we don't actually have that.

Susan Mitchell: I mean, honestly, it's a problem globally, not just with this issue. It's just, as I mentioned, that the pipeline of these interventions that are truly ready are so small, and yet we have this tension of needing to do this work and move it forward, I don't know, quickly. And whether or not, as you mentioned, every aspect of the intervention means adaptation, means going back to stage one, or is there some, depending on the complexity of that intervention, et cetera, is there some, not quite shortcuts, but some fast track that you can do, because there's a lot of work to be done.

Consuelo H. Wilkins: Yeah, I think we also have to ask ourselves a fundamental question about, what are our expectations as they relate to contributing to, or eliminating, inequities in health outcomes. Because if we've developed an intervention and we're so pressed to move to the next step and stage, in part because we're telling ourselves that there are these disparities and inequities that need to be solved, are we confident enough in what we've already created to be sure that we're not actually going to worsen these disparities?

Susan Mitchell: That's interesting. Can you tell me a little bit more about that? Give me an example, or what you mean by worsen?

Consuelo H. Wilkins: Well, so let's say that your intervention is going to be some cognitive behavioral therapy, or some cognitive stimulation that was based on, we'll say a game that was developed in people who speak English, and who are westernized, Americanized, or acculturated, even if they are from some other background or country. And the words in the game are words that are familiar to people who grew up in the United States, and the prompts are based on cultural cues that are really relevant only to people who grew up in the United States and spoke English. And yet we've seen some evidence that, oh, yes, people are maintaining their cognitive function, or they're improving somehow on neuropsych tests based on this intervention, which is just simple, it's a game, and it doesn't cost that much to translate it into Spanish.

Consuelo H. Wilkins: But you are translating word for word, you're not trans-creating, and you tell yourself, you have to translate word for word because the intervention is based on syllables and cues, historical cues, that are really not relevant to this population that you now want to use it in. And the Spanish language is a romantic language, and the number of syllables are going to be different, and a direct translation is not actually going to be that useful. So we could, you could, translate this game and all the aspects into Spanish and then deploy it and find that some of the prompts are actually triggering depressive symptoms, or making people feel more weary about their memory, or potential memory loss. You actually have no idea if these words are even relevant in people who grew up outside of the United States. So maybe your process, or adaptation, is going to consider all of those things and incorporate them, but you still didn't test it.

Susan Mitchell: Right. And I guess there's also considerations of really who's involved in the transformation, so to speak, and the stakeholders, and taking X intervention and making it appropriate and applicable to, let's say, a Latino, Latinx population. It feels like a reasonably big step that has to move beyond just translation to make it appropriate for that culture.

Consuelo H. Wilkins: Exactly. We just finished in the last couple of weeks creating just recruitment materials in Spanish for a study we're doing of amyloid PET imaging, and again, we did not just directly translate, we did a trans-creation process of taking the information that we intended to communicate in English and determining what that would be in Spanish, again, not a direct translation, but what did we mean, or what did we want to communicate? And we still needed to have individuals from multiple countries and backgrounds in Central and Latin America review those documents, that material, because the dialects are different, the words mean different things in different Spanish dialects. So it's a really complex process.

Susan Mitchell: Yeah.

Consuelo H. Wilkins: Which of course is why we want to go quickly. It takes time, it takes time, it takes time.

Susan Mitchell: Well, that's helpful. So let's just move on to pillar three for a second, and that's our trying to build investigator capacity, IMPACT supports career development awards, we have a large training workshop, but among everybody, really, if you're going to do an embedded pragmatic trial, a person like myself, it sometimes usually comes a bit later in the career as a trialist, because that's the stage model, we have to move through it, et cetera. And there's not a lot of investigators in general that fill the intersection between dementia and pragmatic trials and healthcare systems. And so I wanted your advice or thoughts about how to attract, engage investigators, whether it be PhD investigators, or clinician scientists, people of color, of different backgrounds, into IMPACT and into this work.

Consuelo H. Wilkins: Well I hear two issues there, so one is that we need more investigators who are doing research in dementia, and trained and experts in pragmatic trials, period, but that also can do this work with a health equity lens, and I think that group of people obviously does not have to be individuals from racial and ethnic groups that have been minoritized. And then the other issue is we would love to have more people from racial and ethnic minority groups, or minoritized groups, to be in this space, because there is added value in bringing that lived experience to the science. And I like to make those distinct because I think it's important for that latter group of individuals to not just feel like they should be doing work in addressing health inequities and health disparities because they are from these minoritized groups, that we want to value that input and open doors for them to contribute to scientific discoveries across the board. And certainly in Alzheimer's disease, we have so many disparities that we need more people who are doing this work.

Consuelo H. Wilkins: But I think pragmatic trials in general are both attractive from the standpoint of evidence generation, but also a potential concern from the standpoint of health equity. And I brought this up during my presentation, when we talk about real world trials, who's real world is it that we're talking about? In our real world, unfortunately, there are embedded in the structures: racism, disadvantage, and marginalization. So if we are relying on the real world without making some adjustments, adaptations, or considerations for additional data that is needed, then do we really have any chance of addressing these inequities?

Susan Mitchell: Yeah, I mean, I think that's an awesome point, and very on the mark. I often think about the PRECIS wheel and its different domains, and the real world affects each of those spikes on the wheel. So I gave an example during Grand Rounds and it haunts me is that we did a large pragmatic trial in nursing homes where we tried to show a video about advanced care planning to all the nursing home residents during the implementation period, and we found that the white residents were more likely to be shown a video than the black residents. And so the intervention delivery mirrored exactly the built-in inequities and disparities that occur in the real world, and I think we have to really think about that as we think that this is a rigorously done trial, and then we interpret the outcomes in

these different subgroups, but we don't recognize that, in this example, for example, there was inequitable implementation and delivery.

Consuelo H. Wilkins: But that's the real world, right?

Susan Mitchell: It's the real world.

Consuelo H. Wilkins: That's the real world, that is what's happening every day in the real world.

Susan Mitchell: Yes.

Consuelo H. Wilkins: But do we actually know why that is happening? Now certainly we could say there are biases in the implementation, and staff didn't think, or want to, or believe that people could understand it. But it could also be that the residents would not want to watch the video, or consume this information without having their families there, because they make decisions as a family, and that is part of their identity and way of being, that this is not something that they would want to do without their families.

Susan Mitchell: Yeah, so there's this huge added layer of considerations in a pragmatic trial because you are dealing with the real world, then a finely tuned, highly controlled experiment. Even we talk, now I move on to a different part of the PRECIS wheel, but it's subject identification. And so if we're doing it pragmatically, we often rely on an electronic health record, and various algorithms, to identify people with dementia within that healthcare system, because that's how you do it pragmatically. And then if we want to further look at the distribution of minorities, or race, or ethnic background in those populations, we're relying on the EHR, and therefore we're relying on how well those parameters are actually captured in an EHR, and how accurate they are, and what they really mean.

Consuelo H. Wilkins: Right, right, so there are multiple issues in that, in relying on EHR for identification. So one, we know that people who are from racial and ethnic minority groups are less likely to see a dementia specialist, so they're less likely to perhaps have their cognitive impairment documented, and certainly we know they're less likely to have a diagnosis, and even if they do have a diagnosis, that diagnosis tends to come at a later stage in dementia. And so we're not necessarily talking about a population of people that have the same co-morbidities, disease status, level of cognitive impairment, if you're comparing across racial and ethnic groups.

Consuelo H. Wilkins: And then you've already mentioned the issues around documentation of race, ethnicity, and the electronic health records, in general 20 to 30% of health records are missing race, ethnicity, and if you add language there, sometimes that number goes up, in some systems that actually goes down. We are, at Vanderbilt, we're actually better at collecting language data than collecting race and ethnicity data. But is that documented, and if it's documented, are we

confident that people were asked the questions about their identity, or could it have been presumed, or assumed and documented by a third party? So many issues if we're just depending on the EHR for identifying these groups.

Susan Mitchell: There are so many issues, I could talk to you probably for a long time, but we should probably end the podcast. But I really, really thank you, you've given us a lot to think about, and I have a feeling the IMPACT Collaboratory will be calling on your expertise as we move forward and really try to more than move the needle here, but really give some meaningful change in the way we do these pragmatic trials, how they're designed, and how they're conducted through a lens of health equity. So thank you so much.

Consuelo H. Wilkins: My pleasure.

Susan Mitchell: Thank you, bye bye.

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.