Jill Harrison: 00:02 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.

Hello everyone. I'm Jill Harrison, one of the Executive Directors at the NIA IMPACT Collaboratory, and I'm joined today by Dr. Laura Hanson, Professor of the Division of Geriatric Medicine and Director of UNC Palliative Care Program at University of North Carolina School of Medicine, and also Dr. Sheryl Zimmerman, University Distinguished Professor and co-Director of Program on Aging, Disability, and Long-Term Care, as well as the Cecil Sheps Center for Health Services Research at UNC Chapel Hill.

So Dr. Hanson and Dr. Zimmerman, thank you so much for joining me today.

Laura Hanson: 01:06 Thank you.

Sheryl Zimmerma...: 01:07 Happy to be here.

Jill Harrison: 01:08 Great. The NIA Collaboratory hosts a monthly Grand Round series, each with a companion podcast. And this past week, the two of you teamed up for a Grand Rounds about finding pragmatic and relevant outcomes for patients and caregivers in embedded pragmatic trials for Alzheimer's Disease and related dementias. The Grand Rounds was well attended, and there were too many questions to get to in the course of the session. So we're following up today with the podcast, and I'd love to just start. Can you please explain what a patient and caregiver relevant or reported outcome is for our listeners?

Laura Hanson: 01:48 This is Laura Hanson. I'll start out and address that. The focus of our core in the IMPACT Collaboratory is patient and caregiver reported outcomes. And we really have shifted the focus to think about patient and caregiver relevant outcomes. Patient and caregiver reported outcomes are outcomes that are reported directly in the voice of the person living with dementia or their caregiver or care partner. We want to make sure that the outcomes that are used in clinical trials for these individuals

are relevant to their lived experience, they really matter to these people.

Sheryl Zimmerma...: 02:44 Yeah. And this is Sheryl, and I would like to add another reason why that becomes really a critically important point is because, when we're talking about pragmatic trials, there may not always be the ability to take the time to get the actual words of the individual. And so knowing that these are relevant outcomes is critically important.

Jill Harrison: 03:11 Great. Thank you so much for helping define that. So the reported outcomes are in the direct voice of the intended end users or the stakeholders that the research is being conducted with. And then the relevant outcomes, can those be benevolently determined by researchers and health care systems? I mean, how do researchers define the line between co-designing and vetting patient and caregiver relevant reported outcomes with intended end users and stakeholders?

Sheryl Zimmerma...: 03:50 Well, this is Sheryl. I'm happy to start that and then hear how Laura wants to follow up. I don't think that people other than patients and caregivers can be the ones to decide what is relevant. That's the importance of having key stakeholder groups and working in a really close, engaged way with patients and caregivers to understand what outcomes are relevant to them.

Laura Hanson: 04:16 I completely agree. It is one of the things that we're working on in IMPACT and in collaboration with the Alzheimer's Association, is ensuring that we engage the direct voices of people living with this condition in order to help us understand that the outcome measures that we're encouraging investigators to use are in fact relevant to living with the condition and are outcomes that they would like to see improved by future innovations in care.

Sheryl Zimmerma...: 04:57 Yeah. And then if I can add just one more thing to that, is that perhaps for far too long, we have assumed we know what is relevant. There have been increasingly more studies, many have been learned through qualitative methods, that when we think that we know what is important to an individual, like not being hospitalized, like being able to see a family member, that that is not actually what is important, but it's been very kind of consistent with our theoretical models, with our practice models. And when you talk about person-centered care and person-centered measurement, it really is important to go back

and understand whether the assumptions of what we've long thought is important really is.

Jill Harrison: 05:45 That's a great point. Thank you so much for sharing that, the person-centeredness of this type of research. So I think the common phrase is, do nothing about me without me. So that really kind of captures some of the patient-reported and patient-relevant outcomes. I'd like to ask you some additional questions surrounding that. So you mentioned getting the reported outcomes directly from people living with dementia and their caregivers. And in dementia research that seems complex for a variety of reasons, including the progression of the disease itself. Can you talk about the role of proxies or substituted representation in defining outcomes for this vulnerable population?

Laura Hanson: 06:34 This is Laura. I think that that's a really, really important methodologic question for research when investigators are concerned with this population. The way that I'd start to answer that question is to really step back a moment and say that, when someone is living with dementia, this is a disease that inherently means it is hard to do it all on your own. It's a condition where, as investigators, we might be better served in thinking that we're really wanting to consider at least a dyad in our approach to person-centered research and think about including in the research both the person living with dementia and a primary care partner, so that we're confident that we're really capturing the lived experience, which is an experience embedded in relationship as well as individual experience.

That said, your question is really a methodologic question, which is when as investigators should we be using the voice of the person with dementia? And when should we instead turn to someone else's voice to represent their experience, serving as a proxy? Ideally, we will prioritize the voice of the person living with dementia whenever possible, when the condition itself allows them to understand and participate in the research protocol. When we turn to a proxy, it's really important for us to understand methodologically that that individual, no matter how hard they try, will have a perspective that is somewhat different from the person themselves. And we really need more methodologic research to help us understand what changes, and how to adjust for those changes in our conclusions, when we shift from the person to the proxy to ask questions about the lived experience.

Sheryl Zimmerma...: 09:10

And I certainly agree absolutely with everything Laura said. Something that I think is just fascinating about this whole issue of measurement is really the trade-offs. And one has to decide and understand what these trade-offs are. There's a lot of studies that show persons with dementia can be very good respondents, as long as the questions are simple and clear and the response options are simple and clear and that there's not a lot of response options. You wouldn't give a 10-point Likert scale, you wouldn't give a 5-point Likert scale, to someone who would have a very hard time differentiating what 5 or 10 points means.

On the other hand, something that we talked about during the Grand Rounds is that it's important that measurement be sensitive to important changes and clinically significant changes. And as we well know, if you have a limited number of response options usually you have to get a fair amount of movement to get from good to bad, as opposed to getting from level one to level two, level three, level four. So it really does speak to having a very good understanding of what the purpose of your measurement is, what the purpose of your trial is, and understanding how best to, perhaps in a case like this, have responses both from the person with dementia as well as a family caregiver, so that you may get more subtlety from the family member but still understand the overall perspective of the person with dementia.

Jill Harrison: 10:48

Thank you for that. And speaking of trials, as you both are well aware, the COVID-19 pandemic has been devastating to residents in long-term care, especially nursing homes, and more than two-thirds of those nursing home residents have some sort of dementia. So if trialists are wanting to address the pandemic in nursing homes, what types of patient and caregiver relevant and reported outcomes would you recommend?

Sheryl Zimmerma...: 11:19

Certainly one of the many challenges that's happened with COVID is changes in social contact. And people with dementia are, of course, dependent and become increasingly dependent on support from other people. And family members play a very important role, and when those family members aren't able to be there, what we're going to see is well certainly changes in their functional capacity and perhaps their functional outcomes, and also different psychosocial measures. There could be more withdrawal. There could be more agitation. So those types of outcomes are extremely relevant, especially in the time of COVID, because when things are affecting their care and care is no longer the way it typically is, it is going to have functional

effects, physical effects, and psychosocial effects. All of those should and can be measured.

Laura Hanson: 12:19 I love working together with Sheryl because our perspectives are so often compatible but different, and I love that answer, Sheryl. And I was really thinking slightly differently. I've actually been involved in the pandemic for our UNC Medical Center as a point person, helping area nursing facilities navigate their experience with outbreaks. And one of the areas that I've been focused on in that work is the management of physical, as well as neuropsychiatric, symptom distress for individuals with dementia who actually get COVID. Our nursing home colleagues are not sending everyone to the hospital, even though I think some of the hospital teams would feel that way. But they're actually caring for these seriously ill individuals in the nursing facility itself. And so that physical symptom distress that comes along with this illness, nausea, vomiting, diarrhea, shortness of breath, coughing, fever, and the level of distress associated with that, would be one area for outcome assessment. Another area would be advanced care planning and measures attached to effective communication and decision-making in the face of the pandemic.

Jill Harrison: 14:16 You mentioned your work at UNC with the pandemic. And when you think about these embedded pragmatic trials, researchers and trialists, they tend to think of ways how can we leverage existing administrative and electronic health record data collection and processes so that there's not additional burden, so that this information can be collected in the course of normal workflows. What examples and innovations have you seen in healthcare systems to alter their existing electronic health records to capture patient-reported and relevant outcomes?

Laura Hanson: 14:57 This is Laura again. I would say that I think it's too early in the COVID pandemic to say what innovations have been tried. But if we think about innovation in this methodology in general, I think one of the opportunities that's really exciting and that I have seen utilized by investigators is the embedding of very efficient patient or caregiver or clinician proxy-reported outcomes in the electronic health record of a nursing home. I think this is a really great way in a pragmatic trial to bring some of the important outcomes that are really relevant into usual clinical practice and collect the data in the course of usual clinical care.

Jill Harrison: 16:05 I have one final question for you today, for both of you please. So for researchers that are looking to build their competencies

in designing trials with patient and caregiver relevant reported outcome, what types of training resources would you recommend? Where should they start?

Laura Hanson: 16:25 Well maybe this is unfair, but they should start with IMPACT. So honestly, I'm being entirely sincere in saying that I think that there's a great deficiency in training resources for pragmatic trials broadly speaking. But when it comes to working with the AD/ADRD population, when it comes to working with this population in clinical research, I actually think there have been far too few nonpharmacological clinical trials conducted in a rigorous way and almost none that are pragmatic. So I actually think that the training tools that we are building-out as a result of IMPACT and the resources that we are making available to investigators will be singular and not really easily available in other places. And Sheryl, I don't know if you have other insights, but I actually think we're filling a major gap.

Sheryl Zimmerma...: 17:50 I humbly agree with that, Core Leader. I do. But I really liked the question so well because it does show... One of the things that I think those of us who are on the Steering Committee of this Core, I think we have fascinating conversations because many of us have been working in this field for years and years, and other people who've been working in the field of measurement and dementia. And we know that this is a topic that is continuing to evolve. There's work that continues to be done. And there's a lot of very good thought leaders and organizations that have compiled literature about the fact that the measures that exist tend to be deficit-based as opposed to strength-based, and that they might have cultural biases. And they may not, like I said, be sensitive to change, as an example earlier.

So with the question about how can people kind of learn more about this? Absolutely I think that what we're doing within IMPACT is we are putting forth measures, summarizing them, putting them within domains, explaining them. But Laura, we may want to think about also posting some kind of the key literature related to measurement in this field so there could be a resource that people could go to, to help sensitize them to things that perhaps they haven't yet thought about when it comes to some of these conceptual issues.

Jill Harrison: 19:26 Well, we certainly want to direct folks to our website, which is impactcollaboratory.org. And thank you both, Dr. Laura Hanson and Dr. Sheryl Zimmerman, both at UNC University of North Carolina at Chapel Hill. Thank you so much for your time today

		and for diving deeper into this issue of patient reported and relevant outcomes.
Laura Hanson:	19:49	Thank you.
Sheryl Zimmerma...:	19:51	Thank you for having us, yes.
Jill Harrison:	19:56	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.