ACTTION IMMPACT XXV - Patient Engagement in Planning, Conduct & Implementation/Dissemination of CPR

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ACTTION

INITIATIVE ON METHODS, MEASUREMENT, AND PAIN ASSESSMENT IN CLINICAL TRIALS

IMMPACT XXV

Patient Engagement in Planning, Conduct and Implementation/Dissemination of Clinical Pain Research

Virtual Meeting

Friday, October 29, 2021

11:00 a.m. to 2:30 p.m.

C O N T E N T S

C O N T E N T S (continued)

P R O C E E D I N G S

(11:00 a.m.)

Welcome and Housekeeping – Dennis Turk

DR. TURK: Welcome back to all of you who have made it through listening to two days of these presentations. I think they're exciting. I think there's a lot of agreement among the organizers, as well as the chatroom, as well as the feedback we've been getting about how important and valuable this meeting tends to be, or has been, and we hope will continue to be. And I want to express the appreciation that you're able to come back for these three days.

I particularly want to thank the organizing committee, but particularly Chris Veasley and Bob Kerns for the tremendous work they did in identifying the topics, structuring the meeting, and identifying the presenters. I think that they've done a tremendous job, and we really owe them a lot of thanks for doing that.

This is the third day. We'll be winding up today. An important aspect of today will be the

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last part of this meeting, in which we will begin trying to have an outline and discussion about the content of what might go into a research publication, or a publication, that will in fact address the important issues we've talked about. Simon will be running that session, and we'll be counting on all of you to contribute to that.

One point I just want to make before I turn this over to Bob Kerns was, yesterday, Isabel Jordan made an interesting point in which she reminded us that people with lived experiences are different. They're not all the same, and therefore we can't assume that one person or one individual, or even a couple of individuals, will speak for the entire group.

Well, the same could be said about research, and John Farrar reminded us that there's a difference in the kinds of research that we're doing. There's clinical research as a general area, but there are also clinical trials, and there are different constraints on clinical trials that may be somewhat different, and we'll be hearing

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about some of those today. But I think it's important to keep in mind that how we can engage people with a lived experience in certain types of studies may be very different than how we involve them in other kinds of studies.

So let me turn this over to Bob Kerns, and thank you all for being here.

Sorry. I forgot my housekeeping slides. Since we've been over these two times already, they should be familiar to you. We have added and heard what you asked about the chatroom, and we've included and opened the chat room, so that information is available. We are maintaining that information and sharing it so everyone can see it. We appreciate that comment, and if you're finding it helpful, great. It will be open today the same way it was yesterday.

The other points on this slide are exactly the same that you saw, so I won't read them off to you. Carlos, just show the next one; it's the same thing. Notice the importance of Valorie Thompson's email address if you need information about

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anything that we've talked about logistically. She can be reached at vthompson@mac.com.

Now we'll go back to Bob Kerns.

DR. KERNS: Great.

Welcome back, everybody. Good morning. I'm excited to start day 3. And on behalf of Chris Veasley, myself, and the entire planning committee, and of course, Dennis and Bob and the operations team, we all really greatly appreciate everybody's involvement over the first couple of days, and we expect the same today.

I'll make a special request that when you do choose to speak -- and we hope you will speak up, chime in with questions/comments, clarifying questions this morning, and then as we move into discussion this afternoon -- if you would please turn on your video so we can see you when you speak, and remember to unmute yourself.

Then especially during the discussion this afternoon, we'd really like to have more of the feel of a whole group participatory discussion. Maybe at the risk of some bandwidth loss, we'd like

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everybody to turn on your videos. We really strongly encourage -- we've had great participation the first couple days, so we're not concerned about this, but I do want to encourage everybody to feel empowered to share their perspectives, particularly this afternoon as we're flushing out the guts of the recommendations or content for the paper that Simon will be preparing.

Our plan is to go through a few presentations this morning -- you see them on the agenda on the slide today -- and then starting at around 12:45 through 2:30, or however long we choose to, maybe less, we'll spend, really, an open discussion that will be facilitated by Simon with Chris and I helping out. And it's during that time that we'll really be focused on trying to shape up our summary and recommendations in preparation of an impactful publication.

So with that, I'm going to introduce our first speaker. This is Dr. David Leventhal. He's going to be speaking on the How Tos: Special Considerations for Industry Pain Trials.

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Mr. Leventhal is senior director of Clinical Trial Experience at Pfizer, Incorporated, based in New York.

Please take it away, David.

MR. LEVENTHAL: Thank you, everyone.

Bob, can you hear me alright?

DR. KERNS: Yes, we hear you fine. Thank you.

Presentation – David Leventhal

MR. LEVENTHAL: Okay. Terrific. Thank you. And thank you for the promotion. I always wanted to be a doctor, but I'm not.

My background, I've been at Pfizer for 26 years, and I've worked in the space around patient advocacy and engagement for a good chunk of that. I'd like to briskly go through this content and get to a conversation.

I think the most important thing is the story that I'm telling here is one of where you have a lot of individual advocacy around wanting to bring the patient voice into clinical research, and then being able to prove that out with a coalition

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of the willing, and then you build it in an organization, and then you sort of disseminate it out to the rest of industry. And that's very much how this story is going to be told. So I'm telling you the end of the story first.

With that, the importance of partnership, I think, when you're a sponsor of clinical research is that what's driving us is that we have more informed and active patients than ever before; the idea that patient advocates really view the world as there's nothing about us without us activism, and we agree.

We've seen this developing over the years, and internally within our organizations, we have felt that bringing the patient voice in is really important because we've struggled in many cases where in the absence of that patient voice, our programs don't do as well as they could. They have to go back for protocol amendments and other things. So we've always been of a mind that this is something that we should do, but the industry has struggled how to operationalize all this.

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We have those more informed and active patients. We have a regulatory and payer landscape which is demanding it. Our regulators have established expectations. Our marketing approvals are often at risk if we don't integrate the patient voice. Patients are advising payers about which patient-reported outcomes are most important. Payer decisions are going to be at risk if we don't do this, so that is a key component of this importance of partnership.

Then I think at the end, to systematically embed the patient voice into our product life cycle requires a real commitment to standing it up operationally, and the benefit is we satisfy the changing regulatory background requirements, but we're also helping ourselves.

By doing that, as we as say, you speed up by slowing down. And by putting in that additional work before you've finalized your protocol, we're reducing our protocol amendments, we're improving our protocol feasibility, improving retention, enrollment, and adherence, and those types of

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things.

What we needed to do, in 2015, we had to prove this out. Through the Clinical Trials Transformation Initiative -- which is an FDA-sponsored, not just cross-industry collaboration, but cross-sponsor collaboration anchored around Duke University -- we had published a paper around patient engagement practices and clinical research, and got feedback from patient groups, industry, and academia to understand what were the barriers, I think, to engaging with patients.

One of the outputs of that was what we call our Chevron diagram, which really showed where the opportunities to engage with patients and patient advocacy groups existed. And it really wasn't just around our phase 1 through 3 studies. There were opportunities in discovery and in preclinical, around natural history of disease, developing eligibility criteria, endpoints in PROs, and of course in phase 1 through 3, working with patients and advocates around benefit-risk and protocol

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design. These were all pretty clear opportunities.
We also found that in regulatory review, supporting sponsors around those regulatory meetings and giving public testimony in support of regulatory review was really important, and then in a post-approval space in those phase 4 studies to continue to collaborate.
So getting those insights across the continuum was, really, one of the findings of this paper. There were two follow-on papers, one around building and expected net present value calculator, as well as showing that the expected net present value of a research asset benefitted dramatically from getting input from patients and patient advocates.
Now, the link to all this work, I would recommend that everybody go and look at this content because it drove the decisions that we made at Pfizer around how we operationalize this internally.
Our work, we started this work in 2017. We had been getting patient insights into our clinical

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programs, but in a rather ad hoc way. And every time that we wanted to do it, we had to essentially start from scratch. A clinical team would decide they wanted to get patient input, and we would have to develop a whole new set of legal agreements on how to do that. We didn't have fair market value payments established and any of that in place; very hard to do. It took us many months to be able to engage with an individual patient or advocacy group. So it wasn't scalable, clearly.
We set some goals for ourselves in a program, Global Product Development. The first thing we wanted to do is bring together all of the existing resources, which included things like the city paper and other things, and communicate that to the organization.
We wanted to build out the capabilities and the legal framework to make it easier to enable engagement, which for us meant there's going to be a single set of legal templates -- a consulting agreement or a partnership agreement with an advocacy group -- that gets used by the

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organization rather than having to build a new one every time we wanted to do it. Now, that may seem silly that we do that, but this should seem familiar to any organization who tries to do this, that the legal framework tends to be built from scratch every time.
The other thing that we did is we wanted to test all of these tools in several of our clinical programs before we scaled it to the organization. This was kind of like a plan, build, run framework for us, where we piloted all of the work in two to three clinical programs; measured the value and impact on that study; identified any gaps, any recommendations; and then do continuous improvement to make it better.
The result for us is we get a big change management around this in the organization; that every clinical team knows how and when to engage patients and patient advocates in development; that our colleagues in global product development are doing this consistently and it's codified in the organization; that they know how to incorporate the

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feedback and to realize that value to be able to make those protocol changes before the studies are locked down, and get to that place where we have fewer protocol amendments and more improvement in our recruitment and retention, and were all the things that we, I think, said that were going to be a better experience for the participant and better for us, I think, in having studies that meet their endpoints with the least amount of friction.
What we then did as part of our communication to the organization was we created a patient centricity hub, a website for the organization that gives everybody access to the tools. So the other thing is there shouldn't be gatekeepers around this; that we make all this available; and that it enables the study teams to go as a self-service model when it can go and get the tools that they need.
We deployed these tools to study teams to make these partnerships easy. But the other bit of it is we got top-down support from our senior leaders in the organization to ensure that if

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you're going to have your protocol approved by our senior leadership, you have to meet these criteria. These questions get asked of anyone who's coming to our protocol review committee. Have you discussed your protocol with patients and/or the representative; does the protocol have relevant patient-centered viewpoints; and how do the complexity and timing of the treatments or clinical assessments of the duration of participation affect the patient?

If the study team does not have those ready answers to those questions and the data to support it, then there's still work for them to do. So we've made this a core part of our protocol review process.

The next bit of this is we did it as Pfizer, but there's an industry problem around this. We're not the only company that had this challenge, so we were very willing to share, through our cross-industry partnership, TransCelerate -- for those of you who don't know, it is a cross-industry collaboration of 22 large pharma organizations

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looking to solve clinical development problems in a pre-competitive way.

Our view is patient engagement and patient advocacy input. This is a pre-competitive activity, and we think that it is something that everyone should be doing. So we launched this patient experience workstream through TransCelerate.

Again, there are links to all of this work on the following slide. We created a Patient Protocol Engagement Toolkit, which reflects a lot of the best practices that we incorporated at Pfizer. I think the benefits are all the same benefits, but I think they're scaled now, so across industry, you're now seeing a much greater focus on this.

Because many large pharma companies are partnering with one another, if one company is not doing this and another company is, then you end up having some differences philosophically in how we should be offering our protocol.

So there's a whole series of capabilities

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that were addressed in the TransCelerate work and, again, we created a user guide for sponsors of research and created a resource guide, including what we call the Patient Protocol Engagement Toolkit, which includes all sorts of templates and tools for anyone who wants to do this, who's the sponsor of research. All that can be found at transceleratebiopharmainc.com in the Patient Experience space.

Then lastly, I wanted to just make mention that our commitment at Pfizer has never been stronger. The leadership of Global Product Development published an opinion piece in Nature Reviews Drug Discovery last year about how COVID-19 has really forced changes in how we're Conducting research.

We have an accelerated approach now to conducting research within Pfizer, depending on the type of clinical program, and we've made some public commitments around the changes in research that we think are necessary. We are committing that participants on our clinical trials reflect

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the racial demographics of the country's communities that we work in and that we're committing to expanding awareness and access of our clinical trials to improve the experience of our participants. We're committing to share our knowledge, including our data, more broadly with the research community and embracing the digital tools for speed and quality.

None of these commitments I think are possible without input from individual patients or patient advocacy groups. Underlying all of these core commitments that we've made publicly is the idea of getting patient input into the work that we do.

I wanted to keep us on time, so we're right at nearly 25 after the hour. I've gone through all of my content, so what I'd like to do is I want to say thank you to everyone. I know I went over that all very quickly, but I'd like to open this up to questions to talk about any of this and any of the content that's been created over the years. Thank you, everyone.

Clarifying Q&A

DR. KERNS: Well, David, thank you, thank you, thank you. This was great. I learned a lot, personally. I thought I knew something about what industry and Pfizer were doing, so this was terrific.

I want to open it up for clarifying questions or comments, and I see Rick Malamut's hand up first.

DR. MALAMUT: Yes. Thanks a lot, Bob.

David, that's a fantastic talk. I work at Collegium Pharma, and I've been dealing with this challenge my whole industry career as to how to incorporate patient views but also not insult them by telling them, "No, no, no, no."

Just to echo a point made several times, that industry sponsor trials, where the regulators are often your customer, are very different than academic studies, and even different than perhaps post-approval studies, where I think patient input is crucial and maybe a little easier to incorporate.

There a question in here somewhere; it's coming. I actually have two. I'll look at some of what you said, but I have two main questions. What specific topics, what specific areas, did you really focus in on when speaking with patients?

Then the second question is about outcomes. As you gathered this data, how often did you make meaningful changes in protocols and study procedures, and then what were they?

MR. LEVENTHAL: Great question. So again, we do this for every study now, where it's interventional. So all of our interventional studies, we get patient input into them.

I'll give a real-world example, and we've been public about this for our JAK1 study for atopic dermatitis. There were two studies. There was one in adults and a pediatric study. We engaged, through the National Eczema Association, with both individual patients and caregivers. This is a very simple example.

We had a washout period on the use of skin emollients in preparation for participation in the

clinical trial. And if you know anything about atopic dermatitis, the itching can be quite stressful and maddening in many cases. We had a washout period in our study that was deemed to be too long by the participants that we were speaking to, and we went back to the clinical team, and we went back to the IRB, and we were able to reduce the washout period for the use of those emollients to 48 hours from something that was over a week or more.

It's a very small thing, but the parents whose children may potentially participate in this clinical trial said, "Given this washout period, I wouldn't enroll my child in this clinical trial" because of this one particular thing. And this is just one of many things that we do.

The other thing that we do is we do clinical trial simulation under certain circumstances, where we'll actually bring in participants and take them through the daily schedule of activities; not in a real way, but if you have to do -- some of these require a blood draw and a battery of tests over

the course of 6 hours, and in many cases, a participant will say, "Well, I don't think I can do that" and "You didn't really feed me very well at lunch, and maybe I needed something else to get me through the day."

That's just an example of the kinds of things that I think everybody should be doing to really make sure that these are fit-for-purpose results.

DR. MALAMUT: I'm hopeful that you get meaningful input on a hundred percent, but what would you say your average has been? How often do you get something that makes a meaningful change to the protocol?

MR. LEVENTHAL: It's hard to say across the entire portfolio, but we get meaningful input on at least 60 to 70 percent of our studies, where we'll go and we'll make some tweak in our protocol. The nice thing about this, though, is -- as you all probably know -- most protocols are written historically, meaning that a protocol gets typically based on things that were done in

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precedent before it, and many times the eligibility criteria get included in protocols just based on historical precedent, which may or may not be the right thing to do.

We've done some foundational changes based on patient input, where the entire portfolio is affected. We've decided, okay, we're going to take this battery of exclusion criteria out of all of our studies because they're no longer relevant. That makes a big difference, so we've started addressing those kinds of things as well. I hope that answers your question.

DR. MALAMUT: No, that's great. Thanks a lot, David.

DR. KERNS: Thank you. We're going to take two more questions. I hope this doesn't back us up too much.

First of all, Laura Forsythe.

DR. FORSYTHE: Yes. Good morning. That was really interesting, and I think my question actually follows nicely from the previous one.

I was just wondering what conversations, if

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any, you all have about return on investment. As a person, where part of my job is to try to figure out how do we understand and communicate the return on investment of engagement, I'm actually a little jealous sometimes of my colleagues who work in other points on the translation continuum, where there might be more of an opportunity to really talk about return on investment.

I can put an example on the chat of something that the folks at Citi did a few years ago related to investment in engagement versus the return when you avoid terminated protocol or some other things like that. And I wondered if you could speak to beyond the moral commitment that Pfizer has and how you all think about return on investment, and if you're examining that in some way.

MR. LEVENTHAL: Well, we were authors on those expected net present value papers done by Citi, so we believe it. The evidence is there, that by engaging with patients, if you reduce -- just one protocol amendment can run a

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minimum of a quarter of a million dollars. Those are the industry benchmarks we had done in that research. The value is really there.

The other thing that we did is we created that online tool to quickly be able to assess that return on engagement in a way that's really palpable for sponsors. I would recommend anyone to go out and give that tool a try. Then of course, with all models, it makes a series of assumptions. But when we did that work, the assumptions were not crazy. They all more or less made sense, and we're in keeping with what we had seen that CitiCorp had done and our own internal work.

So we don't necessarily have to do the return on investment modeling internally to Pfizer any longer because we've now instantiated it, but understand that there are other places that do. We do a retrospective analysis, though, on each of the studies and say, "What did we change?" And it's hard to do a head-to-head, where we run the study without it and we run the study with, but we try to go back and say, "Well these were things that we

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think were meaningful."

DR. KERNS: Thank you both.

I'm aware of the time, and I want to keep the agenda flowing. I apologize to Isabel Jordan and Sean Mackey, whose hands are up, and there were a couple comments in the chat. If you wouldn't mind saving those until the discussion after the presentations, I'd greatly appreciate it.

Isabel, anything you'd like to ask that's a clarifying question or is it ok to wait?

MS. JORDAN: It can wait till later. That's fine.

DR. KERNS: Thank you very much.

Alright. Let's move on then. Thank you for those comments, and thank you, David, again.

MR. LEVENTHAL: Thank you.

DR. KERNS: Next up is a panel of Regulatory Agency Perspectives in Engaging Patient Partners and Other Stakeholders in the Planning and Conduct of Pain Clinical Trials. First up is Nathalie Bere. She's the patient relations coordinator for the European Medicines Agency in Amsterdam, The

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Netherlands.
Ms. Bere?
Presentation – Nathalie Bere
MS. BERE: Good morning, good afternoon, everybody; a pleasure to be here. I have a few slides to show, so I'm not sure if they can be brought up. Great. Thank you.
I'm just going to share with you some experience that we have at the European Medicines Agency here in Europe for engaging with patients. For those who don't know, obviously, the EMA is the European regulator for medicines across Europe.
It's taken us some years, but we have now developed a whole system whereby patients are now fully integrated in all aspects of our work along the whole medicines regulatory life cycle, through the presubmission procedures, the evaluation of the medicines, and then right on into the pharmacovigilance aspects as well. They are committee members; voting members. They participate in ad hoc expert meetings. We do larger public hearings. There are various

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different ways they get involved, and the next slide will highlight that a little bit.
It's really, as I say, expanded over the years. What we try to do is start out slowly, do pilots, work with the patient community and the patient organization, and work to find out what works best for everybody involved so that it really is an optimal way for getting them on board, obviously, into a rather scientific regulatory arena, but allowing that to be conducive to really get very good information from them and for them also to feel comfortable.
Here, overseeing how they are involved, they're full voting members on the management board on some of our committees. We have a working party of patients for the PCWP. We also have one of healthcare professionals and we often meet together. We have joint meetings with them because we found that, obviously, a lot of the topics are common, and they actually like to be able to hear from each other directly and have a debate, a lot of consultations in writing, workshops, and things

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like that, and then also the individual experts.
You can see here the activity depends on what they represent. Either they represent themselves if they're living with a condition -- and we're talking about a specific medicine assessment, so there they bring their own experience to that discussion or the meeting -- and other times they're representing their particular patient organization, obviously often therapeutic-wise, or they could be representing their whole community as they do in committee membership.
Over the years, the numbers of patients involved has increased. We try to be transparent about this, and we publish every year annual reports. We publish all of the documents, so that it's fully clear how we engage.
I touched upon this a little bit earlier. They really do contribute directly into the scientific discussions. Obviously, their role is different than the scientific experts, but they get involved in the presubmissions; the scientific

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advice procedures; the expert meetings during the evaluation of the different medicines; written consultations; stakeholder meetings; public hearings; et cetera, et cetera.
They also review all of our written information, and I think this is also very important because we need to make sure that we're writing everything in a lay language and it's understandable. So from package leaflets to safety communications, et cetera, they review all of them.
Here, I just really wanted to be a little bit more specific for you, and I think you might find this interesting. One of the ways that they get involved is our scientific advice and protocol assistance procedures. These are procedures where pharmaceutical companies/developers can come to the EMA and ask for advice on the development plan. It's called protocol assistance when they're developing an orphan product, obviously, for a rare disease. That's the only difference.
Patients are involved in a lot of these procedures, so of course we want to see does it

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make a difference, what's the impact, and is there value for everyone involved. So we carried out a survey over the last three years, which involved about 300 of these procedures. We sent out questionnaires to the regulators involved, as well as the patients when they participated. The participation can either be in a face-to-face meeting, or virtual, or it can be in writing. It depends if there is a meeting or if there isn't.

We really asked them to let us know when the patients participated; firstly what kind of things did they bring to the discussion, and then how often did that make a difference. Did it just generate discussion or was there an actual tangible difference to the final advice letter that then is given to the developers?

You can see here, on the right, the different areas where patients contributed, so it really is on tangible points -- sorry, it's probably a bit little -- on endpoints, population, quality of life, standard of care, feasibility of the study, and things like that, so really relevant

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points that they bring to it.

Then, overall, we found that in just over half of the times when patients were involved, comments that they brought resulted in further discussion. So it generated discussion in the meeting, and 20 percent of those cases then actually led to a tangible difference or an addition to the advice that is given back to the company.

Importantly, in 90 percent of the cases when there wasn't a difference, actually we found that when we looked a bit deeper, it was because the patients were actually agreeing with the proposed plan. So I think it's important that it doesn't mean they have to disagree or say something new for it to be an impact for us; it's also impactful that they agree with the proposed plans, and it seems feasible, et cetera, from their side.

I think this is just a really nice example, and it's not always easy to get this kind of data on the value and impact of patient involvement, or any expert involvement. When you're looking at

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these kind of involvements where it involves joining meetings or giving input in writing, it's very subjective to try and determine how much did somebody say and how much impact did that have, but I think here we managed to get some data, which we're going to publish a paper shortly.

We feed this back to the patients involved as well so that they understand that it is valuable having them there, and it does make a difference, and it's not just a tickbox. And it helps us understand, as well, that we're doing it in the right way that is allowing us to get this information in.

I just added another one we do. We do review the number of comments that people make on those documents I mentioned earlier. We did that a couple of years ago, and about 50 percent of their comments made a change to the EPA [ph] summary, which is a document on the oval EMA summary.

In the next and last slide, it was just to summarize that we've developed various ways that patients can engage in the regulatory activities at

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EMA. It does make a difference. They bring data that we don't have: the aspects of living with a condition; what their unmet needs are; and what they're looking for in a new treatment or a new medicine that helps bridge that gap. It allows us to be transparent and gain trust as well with patients and with the community.

So yes, value demonstrated, and I think at the end we've seen that it does lead to, hopefully, more meaningful outcomes for everyone. So that's my slides. Thank you.

DR. KERNS: Thank you very much, Nathalie.

We're going to go right on to our next presentation, and we'll have three in this series, and then come back to questions after that.

Next up, actually, is Captain Robyn Bent. Captain Bent is director of the Patient Focused Drug Development program in the Center for Drug Evaluation and Research at the FDA in Silver Spring, Maryland. Captain Bent was uncertain about her ability to get here for this presentation, so actually we have a pre-recorded presentation from

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Captain Bent.
Carlos, if you'd cue that now.
Presentation – Robyn Bent
CAPT BENT: Thank you so much for having me. I'm Robyn Bent. I work for the Center for Drug Evaluation and Research's Patient Focused Drug Development program here at the U.S. FDA, and I'm really happy to be here to talk to you today about FDA's focus on including the voice of the patient in medical product development and our perspective on the importance of patient centricity.
I'm going to talk about how we're encouraging that, and then I'm going to move on to talking about the value to researchers of adopting a more patient-centered approach to drug development and drug safety from FDA's perspective.
Before I talk about patient-focused drug development, I'm going to define it. Patient-focused drug development is really a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and really meaningfully incorporated

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into drug development and evaluation. I'm going to start by framing the conversation.
The purpose of this slide is to really show some key areas where patient input can be valuable, but this isn't to imply in any way that these are the only areas in which patient input can be valuable. For example, in the early stages of clinical development, patient input can help researchers and FDA really understand what impacts of a disease and of treatment matter most to patients and help us figure out how to best measure them.
During the planning and conduct of clinical trials, patient input can help us to understand what aspects of clinical trials can be better tailored to meet the needs of patients who may participate in the trials. During the premarket review stage, we can use data obtained directly from patients, such as patient-reported outcome measures or patient preference studies, to inform FDA benefit-risk assessments. In the postmarket setting, patient input can help us to understand

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how to best communicate information to patients and prescribers in order to facilitate decision-making.
While FDA has a long history of patient engagement, our Patient Focused Drug Development program really began with our patient focused drug development, or PFDD, meetings. We hold these meetings to hear directly from patients, patient advocates, and caregivers with a specific condition about the symptoms that matter most to them; the impact the condition has on patients' daily life; patients' experiences with currently available treatments; what patients would value most in a new treatment; and what factors they would consider when determining whether or not to participate in a clinical trial.
These meetings also have the potential to address areas of unmet need for the patient population and to give us an idea where we might need to identify or develop tools that assess benefit of potential therapies. It can also raise awareness and channel engagement within the patient community.

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What we've heard from these meetings really reinforces that patients are experts in what it's like to live with their condition. We've learned that the chief complaints we hear at these PFDD meetings are often not being factored explicitly into drug development plans, and that, often, they're not being measured in clinical trials. We've learned that patients want to be as active as possible in the work to develop and evaluate new treatments, and that the most obvious symptom of a disease or illness is not always the most bothersome.
One example of a meeting that we held was a meeting on chronic pain, which was held back in 2018. For our chronic pain meeting, we had more than 120 patients and caregivers in the room and over 300 participants online. We received over 2400 comments to our public docket.
In order to get this level of participation, we reached out to a number of patient groups and medical facilities, asking them to share information on the meeting with their members. We

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worked really hard to accommodate our meeting participants so that they felt they could attend the meeting. We heard from patient groups that participants may need areas to rest or to lay down in the event that their pain got overly severe, so we reserved additional rooms to support them, which are things that we may not have thought of if we hadn't worked with the patient groups and really listened to their feedback. The Voice of the Patient report from that meeting is available on our PFDD website.

In addition to including patients in the drug development process itself, FDA also encourages the inclusion of patients or their caregivers when developing fit-for-purpose clinical outcome assessment, and this is critical. And not only do we talk about the importance of doing this and have an entire guidance series focused on it, we're actually doing these ourselves.

As part of our Standard Core Clinical Outcome Assessments and Related Endpoints Grant Program, we're funding the development of a core

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set of measures to assess acute pain in infants and young children. This program really leans heavily on the feedback from patient caregivers who work with our grantees as active members of the team, as members of the external technical advisory committee, and of course other caregivers who are currently participating in the qualitative concept elicitation portion of the grants.

So while you're reading this, I just want to talk a little bit more about the value of patient input because in addition to improving the science of clinical research, it can have other effects. There's literature that supports that working with patients and patient groups can decrease trial attrition.

It can increase understanding of barriers to trial enrollment and participation and increase researchers' ability to recruit diverse populations. It can increase the rate of enrollment into trials, and it can decrease the number of protocol amendments by identifying potential problematic exclusion criteria or aspects

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of the protocol that may decrease willingness of patients to participate in the trials. I think this is all really important information.

Finally, this slide provides you with a link to our Patient Focused Drug Development home page, as well as a link directly to our FDA-led PFDD meetings. Thank you so much for your time, and I look forward to your questions later in the meeting. Thank you.

DR. KERNS: Terrific.

Next up, we're going to hear from Dr. Alysha Croker. Dr. Croker is the manager, Office of Pediatrics and Patient Involvement; the Center for Regulatory Excellence Statistics and Trials, or CREST; the Health Products and Food Branch of Health Canada, Government of Canada, based in Ottawa, Ontario, Canada.

Dr. Croker?

Presentation – Alysha Croker

DR. CROKER: Wonderful. Thank you so much.

Hello, everyone. Thank you for including Health Canada in this panel discussion. I'm really

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honored to be here to talk to you a little bit about Health Canada's patient involvement activities. As a note maybe just at the beginning, Health Canada has just started its work in this area, so as you'll see, some of our slides were not quite as far ahead as the FDA or the EMA on this topic.

Just quickly for those of you who may not be familiar with the internal structure of Health Canada, I'll just take a second to orient you. For those who are aware, Health Canada's responsible for helping people in Canada maintain and improve their health, and we do this in a lot of ways. One of those ways, of course, is by regulating the import and sale of drugs in Canada. That's the Health Products and Food Branch that acts as Canada's health regulator and is the branch that's responsible for authorizing health products based, of course, on their safety, efficacy, and quality.

My office, the Office of Pediatrics and Patient Involvement, is within the HPFB, or Health Products and Food Branch, and we work across the

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branch and a number of files, including integrating patients' expertise across our regulatory and policy work. Robyn's already talked a little bit about patient-focused drug development. I've put devices in there, too, because I think the premise of PFDD applies to medical devices as well.

Just to mention quickly, there's obviously an increasing need to draw on patient knowledge, experience, and expertise in order to really understand the day-to-day realities of living with a particular disease; what the comfort level of patients with this disease might be to risk; what clinically meaningful endpoints look like to these patients; and whether unmet medical needs are being met through a particular drug, or device, or trial, and that type of thing.

Robyn also had a slide very much like this, so I don't need to go over this in much detail, other than to say that there are a number of ways and places that patient-focused drug and device development can be integrated across the life cycle. Focusing on trials, here I've bolded the

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text in aqua just to draw your attention to a couple of examples.

As I mentioned, Health Canada's patient involvement activities are still in the initial stages. We're in the process of pulling together a patient involvement strategy, which will aim to have regulatory and policy decisions being formed by the patients who are impacted by those decisions, and then we'd aim to accomplish that by finding ways to systematically integrate meaningful patient involvement activities across the drug and medical device life cycle.

As we've already heard from the previous panel members, we have a lot of wisdom and experience on this topic internationally. Both the FDA and the EMA have already implemented wonderful patient activities that we now have the benefit of learning from in Canada.

In terms of pain, Health Canada doesn't currently have any ongoing patient involvement or initiatives related to that topic, but we're always open to working with patients in the broader

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community to identify and address issues that fit within our mandate and that are meaningful to patients. So I'll stop there, and I look forward to the discussion.

Clarifying Q&A

DR. KERNS: Thank you, Dr. Croker, very much.

Let's take one or two questions before we move on to our next presentation, and try to keep them to clarifying questions if you can.

Lee Simon?

DR. SIMON: Hi, everyone. I was wondering, as it relates to EMA in particular, in that you all incorporate patients into some of your scientific discussions, how do you vet them for potential conflicts of interest to be able to participate in such a thing?

The FDA on advisory panels goes through a whole series of complicated vetting procedures to ensure no conflicts of interest. How do you do that for your individual scientific committee meetings as you use patients and incorporate

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patients into giving such great advice? How do you do that?

MS. BERE: Well, thank you very much for the question. Yes, indeed, we also have a whole system of vetting individuals before they can get involved. They have to fill in various forms. We have a declaration of interest form, so they have to highlight any interactions or any interests they have with pharmaceutical companies, they or their families, or any links, which is then submitted.

They have to fill in other various forms, and essentially they have to become what we call an EMA expert. These forms are then put into an expert database, and then actually we do publish all of the experts' names and certain level of detail so that we're transparent.

If they become an expert, this lasts for a year and they can renew it. And then each time we have a specific activity, their declaration of interest is then reviewed for that particular activity, that particular product we're talking about, again, to make sure there is no potential

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conflicting interests.
So hopefully that answered your question. We're lucky that it's a pretty online system. It does still take some time to do, but it's an online system of various forms to fill out.
DR. KERNS: Thank you. Thank you, Lee, for the question.
Penney Cowan? We'll take one more question from Penney, and then we'll move on.
Penney?
MS. COWAN: Thank you. And thank you, all, for your presentations. I have one for Ms. Bere.
The people that take part in your panels are not your average consumer. So my question is, do you ever go out into the communities once they review all the materials, the past [inaudible – audio gap] -- focus groups, and inner cities, and rural areas to see if they also understand and comprehend the kind of information -- I mean, the very end user, and they're not the ones -- they're the ones who are probably taking it or choosing not to, because they read -- I mean, do you ever go out

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into the communities and do those focus groups to really get their feedback? Thank you.
DR. KERNS: I think the question may have been for -- yes, please?
MS. BERE: Was it for me? Sorry. I didn't hear --
DR. KERNS: Well, I think anybody, but --
MS. COWAN: Yes --
(Crosstalk.)
DR. KERNS: -- I think she called you out.
MS. BERE: It was? Okay. Thank you.
MS. COWAN: I was trying to do it quickly.
MS. BERE: Sure. No. Thank you for the question as well.
We actually do try to reach out to the community. I think it's really difficult to get to the hard-to-reach patients, so we rely, on the one hand, on the patient organizations across Europe. They really have a good outreach with the patient community. When we get them to get patients involved, we also try and tell them to reach out, really as much as they can, within their community.

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So whenever we have an activity and we're advertising for it, to reach out to those patients as well.
We also have a registration system for individual patients. Not everybody is part of an organization. We also try and use social media and things like that to reach out and get the individual patients to register in a database that we have; and then when we have these activities, we then try and do a mix of reaching out to the individuals, and then also reaching out to the organizations.
We have a big challenge in Europe in terms of language because, of course, our working language is English, and in Europe there are many different languages spoken. So I would say that that is a key challenge as well.
DR. KERNS: Thank you very much. Thank you for the question, Penney. We'll have more time for discussion; just a great panel. Thank you each for terrifically focused and comprehensive presentations.

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I'm going to turn next to our next topic on the agenda. This is the how tos related to Measuring Patient Engagement in the Planning, Conduct, and Dissemination/Implementation of Clinical Pain Research. This will be presented by Dr. Laura Forsythe. She's director of Evaluation and Analysis at the Patient-Centered Outcomes Research Institute, PCORI, in Washington, DC.
Dr. Forsythe?
Presentation – Laura Forsythe
DR. FORSYTHE: Thank you very much.
Well, I guess we've just moved to afternoon on the East Coast. Good afternoon, everyone. It's a real pleasure to be here. On a personal note, I'm actually thrilled to be presenting at a meeting focused on pain research. While I'll be, really, drawing on my experience in this talk from my nearly decade at PCORI, I actually started my doctoral training to be a clinical health psychologist, studying management of chronic pain with Beverly Thorn. So more than usual, I wish this meeting was in person because there's a bunch

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of you I'd love to say hello to and catch up, but here we are, measurement of engagement in research.

What I want to do is try to explore four questions about measurement of engagement in research: why is it important; how is it complex; where are we now as in what do we have with respect to measures; what do we know; and then what does it mean for us? And, really, I'm thinking "us" as research teams in the field, as PCORI and other funders, and as a collection of colleagues trying to advance clinical pain research.

There are kind of three main sources I'm going to draw on to talk with you about this today. There are two systematic reviews about measures of engagement, one by D. Bowen and colleagues from 2017 and another by Antoine Boivin and his colleagues in 2018.

PCORI has in progress right now a landscape review and gap analysis about measures of engagement in research, and we're trying to answer basically three questions there: What measures are needed for and by whom? What's the current state

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of measures available and how do those aligned with stakeholder needs? And then, how do we address measurement gaps? We commissioned this project and collaborate on it with Tom Concannon and his colleagues at RAND.

How we are learning about measures through this project, there are three core components: key informant interviews with a diverse set of stakeholders that have experience and interest in measuring engagement and research; literature review; and then coming soon, a synthesis of all of that.

If this meeting were in another couple months, I would have, even then, a lot more to say, really, about interpretation of where we're at with measures, but I'll give you some early lessons so far. We engage patients and stakeholders throughout this project, particularly through a multistakeholder project advisory group that advises on each stage of the work.

I want to talk a little bit, briefly, about why measurement of engagement is important. I

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expect you all actually already have your own ideas about this, but I think it's helpful to start with some of the grounding assumptions that I'm bringing to this conversation. Just as a reminder, you heard from Dr. Goertz and Dr. Carman from PCORI on the first day of the meeting about PCORI's expectation that engagement to us means the meaningful involvement of patients throughout the entire research process.

You heard them talk about how PCORI expected that engagement would lend research that is more relevant, high quality, and more likely to be used in decision-making. You also heard what we know so far about engagement approaches, how to do it well, and the impacts engagement can have and the evidence gaps that remain.

I think that's really the background of why engagement is important, but then measurement of engagement really is a critical tool both for engagement science, studying engagement systematically, and also for the practice of engagement.

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We need standardized, validated assessments to help us move from a conversation about lessons learned and promising practices to more evidence about the most effective approaches to engagement that are acceptable to the people involved and aligned with their values and needs and preferences and the needs of research. People committed to engagement really also still want to understand how to best do it so that we can maximize the benefits of working together.

We also need these measurement tools to help further our understanding of the impact of engagement, not only in the research, but the people involved and health care and health outcomes. This is not only for skeptics who want to hear more about the costs and benefits and risks, but even in the context of commitment to engagement as the right thing to do, this kind of information really can help us understand what success might look like and how we get there.

When we think about engagement practice, measurement is really critical to helping teams

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understand how well they are engaging, are things playing out as they intended, and where can they improve. It's really a valuable piece, ultimately, to help facilitate making engagement easier and more widespread.

Let's talk about how is it complex. I just want to acknowledge that all measurement is complex, but I want to give you some insights specifically into how measurement of engagement in research is complex.

First, we've heard a lot at this meeting about the wide variation in engagement terms, definitions, and approaches. We know that the requirements, guidance, and assumptions about what is sufficient, what is normative, and what is acceptable, those are different for different funders, different consumer groups, and others involved.

Engagement by design is tailored to cultures, to settings, to research areas, and that's necessary and helpful variation. Also, all those differences affect how people think about and

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can see of engagement, what they feel should be measured, and how it should be measured.

Another thing to think about is it's tempting, but we've learned it's not really accurate to put whole teams or whole projects in one single category about engagement, successful or engaging like this, because engagement is also dynamic. It varies over time within and across projects.

It's a bit stating the obvious, I think, but I just want to remind people that in the context of measurement, engagement is affected by factors at multiple levels. We have people interacting together on teams working in the context of projects or research programs; working within and across different institutions, cultures, and funders, and all of those things play a role.

Of course, measurement of engagement, like engagement, is a multistakeholder process, and there are a couple of things to highlight here. The first is that different stakeholder groups have different priorities. They have different

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questions about engagement and different priorities for what gets measured, how it gets measured, and how that information is used.

There are of course questions that span stakeholder groups, but there are also different lenses through which different stakeholders look at these kinds of questions. For example, many patients went to understand if they can have a meaningful impact on the research and the extent to which they felt supported and prepared to engage as they intended. Many researchers have questions about how do I do engagement effectively and efficiently and how will it affect my research in a more proximal sense. Policymakers often have questions about how inclusive is engagement, how do we make it more inclusive, and what's the impact of engagement on health, more broadly.

Also, just to keep in mind that perspective matters, when you have people from different perspectives involved in dynamic situations, they may be coming from different places, different backgrounds, and different value structures. As we

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move forward with measurement of engagement, it's really critical to think about whose perspectives are we capturing; whose perspectives matter; how and why might they differ; and what do differences in perspective really tell us.

I want to move now to tell you a little bit about where we are in terms of measurement. Clarity of goals and definitions really are necessary for measurement evaluation. We've talked about not only do we lack a fully shared language about the core components of engagement and what they mean, which is needed to help us better speak to each other about the ideas about what should be measured and what we're really capturing, we also need more measurement frameworks to provide a strong theoretical foundation for measure, development, and application.

One of the steps PCORI is taking through our current project to try to begin to address this issue is developing a taxonomy or an inventory of the concepts within engagement that we feel we need to know about and to help define what they cover,

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how they group together, and why they're important.
We've identified four broad domains, and would just say, as I alluded to earlier, this is a project in progress. So this is a sneak peek, and these things may tweak some, and we've identified four big domains. I'm sharing a couple examples of concepts that map to each of those domains to help give you a sense of what we're learning here.
For example, engagement content really covers the who, what, and why of engagement, and this includes things like the stakeholders and research involved or the underlying principles like equity; whereas context is really about when and where, in a broad sense, and encompasses things like community and culture, as well as things like a research team and organizational structures within which engagement is happening.
Process is really about the how. These are things like group dynamics, power sharing, and the intensity of engaging activities. Outcomes is about the so what that we've been talking about in terms of things, including the patient and partner

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experience, the impact on research, and ultimately as well on researchers, research institutions, and patient and population health.
Two things to note here is, first, the taxonomy is really just a start. We are not yet at the point of a measurement framework or model that would really give guidance or expectations about what must be measured, how it must be measured, what must be achieved, but this is a start toward some shared language.
Second, even talking about shared language is actually really tricky because one of the things we've learned from our project advisory group and other work in this project is that one person's process is another person's outcomes, and I think that's, again, back to perspective. Kristin, who you all heard from earlier, has been really helpful in pointing that out.
So where are we now? The big bottom line is there are really limited measures of engagement and research available right now. Our estimate of our project in progress is there's about 35 to 40

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published instruments. The majority are drawn from community engagement, and most focus on engagement processes and contexts. Relatively few focus on outcomes.
Among that set of measures, there are some really meaningful limitations. Few report validity testing at all. Most that do focus on face validity. Other forms of content and measure validation are rare. Reliability testing is also rare, and there's really limited grounding and conceptual frameworks.
I want to give you just one illustrative example of a measure that has gone through relatively more validation. This is really a spotlight on a PCORI project. Dr. Melody Goodman has led an effort to develop the research engagement survey tool and just published a short form in 2021. It assesses aspects of both quality and quantity of demonstration of engagement principles, things like sustainability and co-learning. Measure allows us to make comparisons of partner engagement across and within studies

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over time, and stakeholders were involved throughout the conceptualization, and development, and validation of these measures.
Another key thing about the measures that are available now, though, are there's limited measures that engaged patients and stakeholders throughout the entire process. At least historically, many measures either lacked that engagement in the measure development or the engagement is really focused on a pilot phase. It was a very narrow use of partners in terms of thinking about the entire process, conceptualization, design, validation, and implementation. There are some more recent published examples that did a really good and thorough job of engagement in the measure of development, and I have some reference lists that include some of those at the end.
Of course, knowing this, there's also a gap between what stakeholders want to measure and what they can currently measure. This is both because stakeholders are particularly interested in both

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engagement of process and engagement outcomes, and measures are really only focused on the process piece. It's also because even when we think about available measures within process, they have the limits that I was just discussing.

I want to spend just a moment telling you about where we are now with respect to measures of engagement in clinical pain research specifically. I think it won't be surprising that while there are examples of engagement in pain research where the engagement is strong, the science of engagement in measured development is limited in the context of clinical pain research specifically. So it's really an opportunity to ask ourselves what from other settings is generalizable or transferable to pain research, and what elements, if any, are really unique to engagement in pain research?

I would expect that there are a lot of core elements with respect to measurement of engagement that might be generalizable and that there are some unique things we might think about in terms of outcomes, for example.

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Relatedly, I do want to also put a nod to our colleagues in other fields. PCORI really focuses on clinical effectiveness research, which is very far down the translation continuum, but there are colleagues on other points on that continuum that are also helping to contribute to this conversation in ways that are relevant to pain research. For example, the group paradigm in Europe is focused on engagement for medicines development and is doing some nice work putting out things like metrics for engagement in measure development that also could be a precursor to then thinking about what we measure and how we measure it.

What does that mean for us as research teams, as funders, and as a field trying to make progress? The first thing I want to highlight is for research teams out there, I want to talk for a minute about creating a culture of continuous improvement. This idea really takes a page from quality improvement models that value teamwork, peer review, recognizing fallibility, and viewing

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errors as opportunities.

I thought that Christine and Isabel yesterday demonstrated those ideas so beautifully. Even in the absence of a plethora of measures about the engagement process, there are still things teams can do to establish this culture of continuous improvement that starts with establishing shared vision of goals, roles, and expectations, and includes revisiting those and maintaining an ongoing dialogue, a qualitative understanding, and a conversation about what did we want to achieve; what was our vision for how we would work together; and how are we doing on living that out; and also, importantly, closing the feedback loop by recognizing the contribution of partners to the projects, very explicitly?

For PCORI, other funders, and the field, there's obviously still more work to be done. Our current landscape review and gap analysis will add to this conversation about the concepts, constructs, and measures, and we plan to next collaborate with stakeholders and technical experts

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to identify and prioritize measures for use and also measure constructs where new or revised measures are needed. Certainly contributions from others, including people working in pain research, can accelerate our progress and thinking there.

Then, we obviously need more well-developed measures of engagement. We need to figure out valid ways to measure important ideas and then do the work to ensure that they are measuring what we intend. We also need to continue to expand on the more recent trends to engage patients and stakeholders throughout the entire cycle of measure, development, and use. As we get into measure implementation and use, we need to take the time to consider what have we learned from those, what do they help us achieve, and how can we continue to improve those measures.

I just want to offer one more invitation to let PCORI know about your priorities for the science of engagement, and in particular because there are questions in this request for information about measure development, use, and priorities

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there. You can respond to that RFI through November 19th.

I will just quickly reiterate the main summary, conclusions, and opportunities. Measurement of engagement is a critical tool for both engagement science and practice. It is complex for reasons inherent to engagement. Different stakeholder groups want to measure different aspects of engagement and often have different priorities. There's more we can do to make progress to prioritize the constructs where we need more measures and validation, and there's, of course, a gap between what stakeholders want to measure and what they can measure.

We need more measures that are well validated, that are developed through full engagement, and that address those priority topics. A shared language and more measurement frameworks will help us facilitate both measure development and measure use.

I just want to end by thanking my colleagues at PCORI, RAND, and our Project Advisory Group.

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They are critical to all of this work and thinking. Then I have a bunch of stuff for you all for later, which includes some summative references that I talked about; other references related to measures of engagement, including some specific measures that are newer and maybe still in the process of being validated; some references from PCORI that are about the science of engagement more broadly because they touched on some topics that have come up throughout this conversation; and some other resources for the same reason.

Some of you all were asking great questions, and I thought, "Oh, this particular resource would help with that conversation," and that's it. I would love to continue the conversation this afternoon and offline, as you are interested. Thank you.

Clarifying Q&A

DR. KERNS: Thank you very much, Laura. . This was just terrific. I'm sure that this is going to help inform our discussions, and ultimately our recommendations. Chris, and I, and the planning committee all agree that issues around measurement at some level are the core of what we need to be doing at this point, so thank you very much.

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We have time. I'll take a question or two.

John Farrar?

DR. FARRAR: Yes. Thank you very much.

Laura, that was an excellent presentation. I wanted to ask perhaps a difficult question. It may well be in some of these measure publications that I'm not familiar with.

What is the outcome of the measure that you're using for participation? What is considered, by PCORI at least, to be active engaged participation? Does it need to go through to actual changes in the protocol or is it some other set of measures? Obviously, it may be dependent on the setting and the time, or the level of research that's being done.

DR. FORSYTHE: I think I hear a couple things in your questions. There's one piece, which is what is PCORI's expectations for engagement in

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our funded projects and what does that look like? That's really about meaningful inclusion of people throughout the design, conduct, and dissemination of the study. Those roles look very different across all of our projects. They're structured in different ways. The teams look different. As Kristin said -- what day was that? Wednesday -- we didn't prescribe exact formulas, but we did put out a rubric with guiding principles and things that we expect the projects to do.

PCORI is not yet at a point of having a measure of an outcome that means success for engagement. I think that comes back to the points about different stakeholders, perspectives, and what matters. We had ideas about some of the ways that we expected engagement to benefit the research when we set out in terms of relevance for end users and things like that, and have done -- it's referenced, in particular, in Dr. Goertz's presentation from the first day -- some work to examine what has been the contribution of engagement to our projects to things like relevance

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of the project, feasibility, and acceptability to patients and people who would be participants.

So that's important, that we are committed to looking for an understanding of how is engagement contributing. I think the million-dollar question that we're moving into next is how do we really devise a variety of outcome measures for engagement that cover the whole range of outcomes that matter to stakeholders with respect to engagement.

It includes the research project and the design and conduct of the project. But it also includes many things beyond that related to the people involved; the experience they had partnering on the project; their researchers, who they are, how they go about research going forward, and the culture of the institutions; and things like that as well.

DR. FARRAR: Yes. I think it fits with your comment, which is, I think, key here, that it's complicated. Meaningful and what matters, it's sort of a I know one when I see one, but it's

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really hard to define. And I'm simply pointing out that it could be really hard to come up with a single measure, or even a set of measures, that gets at those features.

DR. FORSYTHE: I think that's a great point, too, that I didn't make explicit, is that we are not in pursuit of a single measure of engagement. It's really a constellation of things that are relevant at different points through a project life cycle, or program of research life cycle, or a relationship between groups of people who are working together.

DR. FARRAR: Yes. Thank you very much.

DR. KERNS: Thank you very much, both of you. And thank you particularly, Laura; a great presentation and discussion, and we look forward to everybody's participation in the relevant discussion later.

We have one last session. This is a panel presentation focused on Journal Reporting on Patient and Other Stakeholder Engagement in the Planning and Conduct of Clinical Pain Research.

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I'm pleased to welcome Dr. Mark Jensen. Mark is professor and vice chair for research, Department of Rehabilitation Medicine, University of Washington, and editor-in-chief of Journal of Pain. He's based in Seattle, Washington.

Mark, please go ahead.

Presentation - Mark Jensen

DR. JENSEN: My comments are going to be very brief. I'm just going to make a few basic points, and then hopefully that will leave time for discussion about issues around reporting and participation in stakeholder engagement in papers.

Just key issues to cover, in our journal we want to, and we do, publish papers that report the findings from research of the highest rigor, so rigor is key. The impact of the paper is key, and the methods and results must be clearly and transparently described. Those are, really, the key issues.

With respect to stakeholder engagement, then, we know that clinical research does not always have to have stakeholder impact to be both

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rigorous and impactful, but it often will. As Dr. Forsythe was talking about, it's key to the impact and rigor of many, many studies.

We know that stakeholder involvement is increasingly expected by sponsors. The Administration for Community Living, which funds a great deal of our research, requires that researchers involve stakeholder groups. It's simply a requirement and it's part and parcel of how a project is put together.

As Dr. Forsythe was talking about, PCORI also expects it. It's a piece of it. And as more and more pragmatic clinical trials are being conducted and reported, stakeholder involvement is generally expected to be a big part of the pragmatic clinical trials as well. So we're going to be seeing more and more and more of this because it increases the rigor and impact of our clinical research.

The third key issue is that all the methods and procedures in a study need to be clearly described so that readers can understand exactly

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what you did and can replicate it, if needed. When stakeholders play a role, that role must be described, as expected, in any paper. It needs to be clear, thorough, and brief.

In thinking about this, I think about the person who's looking for a small house with big rooms, and lots of them. In any paper, we want to have it be very thorough and very clear, and we want it to be brief, and that's always the challenge, to make all that work. But you read paper after paper in our journals, and you see that it's successful.

As a tip, there are no word limits in the methods sections, both in the Journal of Pain and, as Frank may talk about, in Pain. So you have the room to discuss exactly what you did because the methods, and being able to understand what you did, and be able to replicate it is so important. But please don't take advantage. Don't just go on, and on, and on. Really think about how you can clearly describe what you did briefly, and remember that, certainly in the Journal of pain, many -- if not

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most, if not all -- journals now, allow for supplementary material and a wonderful place where you can describe in detail exactly what you did as the protocol.

Again, more and more sponsors are requiring that a protocol be completed, approved, in place, and dated prior to even enrolling subjects. If such a protocol exists, then you can make that available to your readers, and that's where you could describe more details about your procedures for stakeholder engagement. So those are the key points that I wanted to make.

DR. KERNS: Thank you, Mark. Perfect.

We're going to next hear from Dr. Frank Keefe. He's editor-in-chief of Pain. He's a professor in psychiatry and behavioral sciences, psychology and neuroscience, anesthesiology and medicine at the Duke University School of Medicine in Durham, North Carolina.

Frank, please, take it away.

Presentation – Frank Keefe

DR. KEEFE: Thanks, Bob, and thanks to all

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for the opportunity to participate in today's session.

Publishing really matters, and reporting what you do really matters. You may have done some wonderful things, and a lot of those have been outlined today, and I'm sure on previous days, to facilitate stakeholder or patient involvement. But unless that is written and gets published, it's not likely to have the impact that it might otherwise have.

So reporting on this is an extremely important topic, and I want to echo a comment that Laura made of how perspective really matters. I think that many of us have hold of this elephant, and we have different parts of the elephant. You probably all remember the story of the blind man and the elephant with various blind men handling different parts of the elephant, and claiming they knew exactly what the elephant felt like or is.

"It's like a hose," said the guy with the nose. "Oh, no; it's like a wall," and so on. Fortunately, one of these wise men was very blind

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and he said, "Let's listen to each other. If we put our thoughts together, we're really going to understand what this looks like."

I think these types of meetings that you're having here are so important because it allows us to listen and talk to each other. And I'm impressed by the consensus of what should be happening in this field.

What I want to talk about, though, as an editor is, what do we see? What is actually happening in the world of publication, particularly with regard to pain and reporting of stakeholder involvement?

What we typically see in pain for clinical trials is randomized-controlled trials reporting the main trial outcomes. That's what comes into us. In fact, many people consider publishing these types of reports to be the primary paper that comes out of a clinical trial.

When those come in, they go out to review for reviewers who are experts in randomized clinical trials and various issues regarding the

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intervention and so on. What those reviewers are typically focused on are things like, was the study pre-registered? Were there multiple study sites? What was the control comparison? How about the evaluations that were used? And so on and so forth. They get very, very focused on this. And if they happen to be a really informed reviewer, they might be looking for evidence in each of these areas; has there been key stakeholder involvement?

Some of the concerns, though, that reviewers will bring up, who have that perspective is -- and I think Mark alluded to this -- was there a description, even a brief description, of how stakeholders were involved? Was that description clear? Did the authors build a case at some point -- maybe in their introduction -- of why stakeholder involvement was important? How is the involvement accomplished? How much of an impact did it have and can it be replicated? If somebody tried to do the study again with a different group of stakeholders, having input across the study design, would it look similar or would there be a

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different outcome?

The point I want to emphasize -- and this is particularly true of many prestigious, high-impact journals -- is, the problem is you're trying to cram an awful lot into that outcome paper. Mark mentioned the methods section. And you do have room there, but probably not the room to really show, if you were very committed to stakeholder involvement, the sophistication and breadth of things that you did to really improve your study.

People really feel kind of crammed for opportunities. I think one of the key issues here to keep in mind from a publication perspective is that, traditionally, this is what investigators often get focused in. "I want to get the primary outcome paper. I want to get it in the New England Journal, or JAMA," or wherever it might be. And they're so focused on this when they think about stakeholder involvement and, "How do I possibly convey the sophistication that I attempted to use in pulling this together and getting stakeholders involved in that primary outcome paper?" It's

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hard. It really is hard.

However, if you take a somewhat different approach, that is one that views this primary outcome paper as one of the suite of papers that could be used to highlight the role of stakeholder involvement, then I think you have a much more balanced approach.

You could write a review paper, building the case for not only the study but why stakeholder involvement was so important; a protocol paper where you describe how the stakeholders, the patients, actually influence the way the study got put together. If your study involves particularly a behavioral intervention, you might want to have a paper that describes the intervention technique. You might want to have a manual and highlight the parts that feature stakeholder involvement, and so on and so forth.

The point is that there are a variety of routes. There are a variety of avenues to highlight stakeholder involvement and to publish reports of that stakeholder involvement. Clearly,

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the primary report is important, but I think that, typically, the limitations of all the other things that you want to address in detail permit, really, displaying the sophistication and the rigor with which you may have approached stakeholder input into your study.

I think that's my last slide. Yes.

Clarifying Q&A

DR. KERNS: Beautiful. Thank you very much, Frank.

Any clarifying questions for either Mark or Frank?

Chris, go ahead.

MS. VEASLEY: Yes. Thank you for those talks; very informative. Some of the investigators involved in this meeting, and others that we've heard from, have been discouraged by the fact that some of their publications were asked to be revised, or flat-out rejected, when they go into detail about stakeholder involvement in their clinical research.

I guess my kind of provocative question to

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you, Frank and Mark, is why should an investigator have to make a case for why stakeholder engagement should be included in their publication? I would think that it would actually be the opposite, that if they didn't, they need to make a case for why it was so.

And I'm not talking about all types of research -- cross, basic, and whatever -- but particularly clinical pain research, particularly since funding agencies are now requiring this to be a part of clinical research when it's included in funding announcements and other areas.

DR. KEEFE: Well, you know, Chris, this is a process, and I think this meeting is part of that process of educating people in the field of what is needed, particularly with regard to stakeholder involvement.

In defense of the people looking at this work, reviewers and so on, they have been educated about a myriad of things that are important. We could go through all the different criteria for clinical trials. There's a myriad of things that

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they need to focus on. And stakeholder involvement may be there, but it's not emphasized as much as some of the things they typically look at.

I think the way to move the needle is to educate people, to raise the status of this. That being said, I don't think any one publication -- for example, the primary outcome paper -- is the only way to highlight what has been done or necessarily the best way. So when you talk about people being asked to change, I would ask what papers. Was that a chapter in a book where they were talking about this? Was it a paper where they described the conceptual model that guides their research, and so on so forth?

So, to me, it depends a lot on the type of submission as well. But reviewers need to be educated, and I'm really glad that I was invited to this panel because I think also members of editorial boards need to be enlightened and educated about the importance of this.

DR. KERNS: Thank you, Frank.

Mark, do you care to add anything?

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DR. JENSEN: Yes. I'll just reiterate that I agree with Chris. Again, if stakeholder involvement was part of the study, it must be included. You don't have to make an argument for why; it must be included. The issue more is what Frank and I both alluded to, is how and where. And it certainly should not be left out of the primary people, at least a paragraph. And if you want to go in great detail, that's fine, but maybe for supplementary material for that. So put it in there, would be my point.

DR. KERNS: I heard also something I want to emphasize, I guess, in Frank's comment, is that this is a process. I heard a little bit about congratulations or a compliment for holding this meeting, and I think it's a good opportunity.

I thank Bob and Dennis and ACTTION and IMMPACT for supporting this because we're hopeful that, like so much else that come out of these IMMPACT conferences, this, too, will have an impact, and maybe not just moving the needle a little bit, but actually stimulating much needed

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action in the clinical pain research community.

Bob Dworkin, you have your hand up, and then I'll call on John. And I do have a plan to actually call on a couple people who had their hands up earlier for other points to give other people a chance. Then we'll hand things over to Simon, who will lead our broader discussion moving forward.

So, Bob?

DR. DWORKIN: Thanks, Bob, and thanks for the nice comments.

I think this is a question for either Mark or Frank. Of course, both of your journals will require authors to do certain things: disclose conflicts of interest; include a consort diagram; et cetera, et cetera.

Should you also require that in clinical pain research there be a statement of whether or not patients were involved, engaged, in any way? And if that attestation, if you will, is that patients were engaged, there be a brief description of the nature of the engagement? I don't think

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either of the journals require that kind of patient engagement statement, and could that be something that you could include?

DR. JENSEN: I'll just jump in. You know, whether or not a stakeholder involvement is necessary depends on the goal of the study. There are certainly highly rigorous studies in which it's not necessary and there are studies in which it is important.

As I'm thinking about this right now in response, I don't know that you'd need to have a statement that says we didn't do it in this case, and this is the reason, because I think it should be clear; if you did it, describe it. What you did should be clearly described.

So there's, in my view, a general -- if we had an attestation, we'd want to have an attestation of describe what you did. But I think that's there already, so we can discuss it. But it doesn't strike me right now that such an attestation should be necessarily required.

DR. DWORKIN: Well, I just have to jump in,

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Mark, and we can take this offline. I would love to hear examples from you of studies, clinical research in pain, where there would be no potential benefit whatsoever of involving patients, because you were suggesting that there are such studies.

Even, it seems to me, if you convince me that there are such studies, why wouldn't the author add a sentence to the manuscript, saying, "We did not include any patient engagement in this research for the following reason"? I would love to read statements like that. It would be very educational and informative.

DR. KERNS: Christine Chambers had a comment in the chat saying, "I wonder what patients' perspectives would be on this issue."

John Farrar?

DR. FARRAR: Yes. Thanks for excellent talks, both of you. One thing struck me particularly, Frank, that you said and that I'd like to build on, which is that you need to defend in any paper of any randomized trial why you chose a particular outcome, how you chose a particular

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population, and in what way did you decide to do the research? It seems to me that maybe we're drawing a line where there isn't one.

The patients play an important role in the design, the conduct, and the management of trials as they go along, the same as any of the other researchers involved in that process. So if I am reviewing a randomized trial, I would look at the outcome and the reason for choosing that outcome, and a comment that said, "Our patients are members of the committee and strongly encourage the use of this one versus that one because it was more applicable to their patient populations," who have a very strong justification for why that was chosen.

So I think maybe we're doing ourselves a disfavor by trying to say it's something special and different. It seems to me that including patients as part of the research team is just a natural outcome of trying to make our research impactful, and I wonder what your thoughts are, or Mark's thoughts are, on thinking about it from that

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perspective of how choices get made.

DR. KEEFE: I think all the publications relevant to any program of research should highlight this. I think the idea that Bob had is an intriguing one, and it's one that we'll take up at our editorial board meeting, where we're constantly updating our policies for open science and transparency. I think it's a very interesting idea.

But it doesn't just refer to one aspect of the program of research. I think the point you're bringing up is there are a lot of very sophisticated decision-making processes that go on across a trial --

DR. FARRAR: Yes.

DR. KEEFE: -- and I think they all provide opportunities for stakeholder involvement, and I think across a range of publications on a research program, the investigator should do all that they can to emphasize that involvement, the role it played, and how it shaped things.

DR. KERNS: I'm just aware of a busy chat,

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and I'm going to, actually, I think call on Christine Chambers to make her point that seemed to lead to other's comments.

By the way, I'd also note as to this specific question about requiring patient engagement -- I did read it in detail -- that Laura Forsythe put in the chat a link to BMJ's statement about this that seems to maybe strongly encourage maybe it's even a little more than that, so please take a look at that.

So Christine?

DR. CHAMBERS: Yes, thanks. There are so many interesting pieces to react to here. I had just posted on the chat I'd be really curious to hear what some of that patient partners engaged in the meeting would think on this. But I think there's enormous opportunity, from an editorial perspective, to look at different interests; not just being focused on whether patients are engaged in the research that happened, but also in how patients can be engaged in review and editorial processes.

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I also think, for me, it's less about making sure the authors report what they did, which is a hundred percent critical -- that's just part of preparing a good paper and making sure you have that rationale -- but also the responsibility or the opportunity that the journals have in helping to shape quality patient engagement.

When I think about the requirements that have evolved over the years with regards to conducting systematic review, or trials, and the expectations on reporting at the journal submission, I think there's a real opportunity to make sure that the journals are signaling downwards, that this is how we think quality patient engagement could be approached in science.

I will say, as someone who submits often with patient co-authors, that I've had very negative experiences on the journal side. Just even the requirement that an institution be listed for every co-author, for example, has been a major-major challenge. I'm like, "This patient partner doesn't have an institution." But it's

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become a barrier to even submitting the papers. We often get into a lot of back and forth at the copy-editing phase about we must have an institution for this author, and I'm like, "There is none."

So I think we need to think about where are the barriers within the system that you need to facilitate. I am not afraid, as you can tell from some of my provocative comments in the chat over the last couple of days -- I'm not afraid to be a bit disruptive, and I'm not afraid to take those risks, but a lot of really career researchers are. That's not the kind of conversation they want to be having with U.S. journal editors or with the publishing side of things. A lot of patient partners get turned off of the engagement and don't want to participate in the future.

I will just say on the publishing piece, and then I'll shut up, that one of the things that I've learned about engaging with patient partners is the way that we engage as academics. Even our use of email, particularly when I'm engaging with

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youth -- I don't know if any of you have kids who are teenagers, but I have to text my kids to tell them to check an email because they don't use email. But a number of patient partners don't use email, and our whole journal publishing system is very automated and all based on email.

So I think we need to really think about how we make things more accessible and how we can embrace different levels of contribution. I know I had inserted Isabel Jordan and her son in a Lancet commission that was led by Chris Eccleston, and we had lots of conversations about should there be authors on the paper; how will the Lancet manage this? So there are a lot of considerations, but I think we need to be a little bit flexible and a little bit disruptive around our typical processes.

So I've thrown a lot at you there, but those are some of my thoughts.

DR. KERNS: Well, thank you very much.

There are a couple of new hands up, but I am going to take the liberty, before I turn the mic over to Simon, to backtrack a little. And I will

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get to the people that have their hands up now, but I want to start back with a few hands up that we didn't get to hear from earlier.

I noticed Isabel Jordan has made a few other comments in the chat. So, Isabel, you have the mic now if you'd like to make a comment or ask your question.

MS. JORDAN: Thanks very much, Bob.

I'm actually going in the way-back machine to when David was talking about industry, and I was really gratified to see how they were putting in supports for folks in their company to have standards around and tools about how to engage with their patient partners. I think he called it a self-serve model so that they could go and have a standard way, really a common way, of interacting with patient partners.

I think that's really important so people know what they expect when they're interacting with an organization, or a lab, or an industry, or whoever. And I was further gratified to see that they're doing this across industry and sharing

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tools. I think that's so important to create tools for folks doing the engagement work, but I think it's equally important to understand that patient partners need supports as well so that we can support one another.

I'm curious whether he or his colleagues have given any thoughts to providing a similar kind of platform for the folks that they work with in the patient partner world to connect with one another so that they can connect over how their experiences are going as patient partners and to have that kind of shared experience together. Because I think that kind of platform for them to connect would also be really important to create that shared experience and shared knowledge about how to do work well.

DR. KERNS: Thank you, Isabel. I should have realized this, that you're hemming up around David's presentation. He's not with us right now, but he said he was coming back. But I think the point is still very important. It underscored a couple key points, I think, that we're all hearing,

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and I'm sure Simon has captured that. And maybe there will be an opportunity later to raise it again when David is present.

MS. VEASLEY: Bob?

DR. KERNS: Yes, please.

MS. VEASLEY: If I can just weigh in really quickly. Isabel, in our conversations preparing for the meeting, although he didn't include it in his slides, that's exactly what Pfizer's done. They've created kind of an online virtual community for people who have participated in that way throughout their entire research continuum, and also to basically advocate and help each other become advocates, because not everybody has that experience of what it means to be an advocate and how to do it well, and educating yourself.

So maybe he can speak on it a little bit more, but they have done that.

DR. KERNS: Thank you, Chris.

I think next on my list from an earlier presentation was Sean Mackey.

Sean, are you on, and would you like to make

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your couple comments, or question?

DR. MACKEY: Yes. Thanks, Bob. This was related to the earlier discussion around industry, but I think it is a broader discussion as well, and it has to do with how to manage tensions.

By way of example, we're involved with an FDA grant right now to develop a tool around decision-making related to how patients choose between medical devices that may help reduce their pain and may also help reduce opioids. This involves something called the Discrete Choice Experiment, and they have to choose different scenarios. We have to choose outcome measures for this, and we're fortunate to have patient advocates that have been involved from day one on the design aspect, two of which are on this call.

It's wonderful when everything in the discussions go well, but I guess my question is, how do we handle tensions when there's disagreement? What I mean by that is there's going to be disagreement in at least a couple scenarios. One is what happens when the researchers simply

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disagree with the patient advocates over what should be measured and what they think is important?

Then there's a second one, which I think is at least as important, which is, what happens when you agree with the patient advocates that they come up with something that they think is very important to measure, but it's not in line with the regulatory interests and the outcome measures that, for instance, the FDA is interested in measuring, and you simply can't do it?

Now, we're fortunate to have a couple of the people, Penney and Chris, who are on here, who are two of the most grounded people you'll ever meet in your life. So we were able to work through those those tensions and have some really good discussions. But how have people handled this when there are tensions and disagreements? So I just put that out to the group.

DR. KERNS: Thank you, Sean, for that important comment.

I think Chris, the planning group, others,

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this is really an important issue. My own reflections on this is it's maybe not even fair to call it tensions, because -- if we all assume -- people with lived experience or patients come from all different perspectives. They're not a uniform group. There's a huge diversity.

Especially as we promote efforts to enhance the diversity of participation, the participants in these processes, we might expect to see more frank disagreements. Your issue about, ultimately, recommendations that emerge are discordant with, for example, regulatory requirements, that's a key challenge.

I think we can take a couple of comments now around that if anybody would like, but I frankly think that this is a key question for the broader discussion later.

DR. MACKEY: Well, I agree with you --

DR. KERNS: There probably are some specific examples, and I think Laura Forsythe put something in the chat about what PCORI recommends or is a concrete strategy. I didn't have time to look at

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it.

DR. MACKEY: I brought this up just because everything is wonderful when everybody's in agreement; you know, Kumbaya, and we all love those situations. But I think we would all benefit from learning how do we handle situations when there's just frank disagreement or these tensions, and how to navigate that I think is just of incredible importance.

DR. KERNS: Yes. Thank you.

Laura, you want to make a comment?

DR. FORSYTHE: Sure. I was just saying, Bob, PCORI actually has, literally underway right now, a case study project about this exact issue. We had a couple years ago a qualitative interview project with investigators and partners, and then we did a follow-up, in-depth case study with six projects. Our specific research question there was how do people deal with tensions? And that was the word that we brought to the project.

I just wanted to share, we literally were just looking through the analysis a couple weeks

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ago, so it's not out yet. But I can share, first of all, universally, the six studies, the investigators and the partners told us they shied away from that word "tension" and "conflict." They talked about difference of perspective or thinking through different ideas.

I think a key element that came through was some of the projects were very intentional from the start, laying out their decision framework; decision rights; how they approach framework; how they were going to deal with difference of perspective; treating it not as a problem but an opportunity, and coming in when you build that foundation of here's how we're going to work together and here are our roles.

Being true collaborators doesn't mean we can do everything that anybody wants, but being part of that foundation and also talking through what are the rigid bounds and what are the flexible ones; like where are there things -- just the scientific rules, the funder rules, the regulator rules, whatever -- that will not allow this. How else

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outside of this project, then, can we address that issue, and where are there more flexible bounds, where its history, or tradition, or preference that people might be able to think differently about?

I will just also give a nod to a lot of our work in how to do engagement well meets the need for investigators or whomever and is really leading these conversations to develop their facilitation skills. We talk a lot about training for partners, but at PCORI we're also trying to talk a lot about training for researchers, or the team leads, or people because there really is an art to navigating. Difference of opinion is not specific to having patients at the table. There's difference of opinion among well-trained researchers as well, so it's the same strategies of how to navigate those.

DR. KERNS: Thank you very much.

I'm going to ask for some advice of Chris and Bob and Dennis. I'd like to continue this discussion for a minute. Well, it may go on for a few more minutes. There are several people now

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with hands up that want to make comments. But I also am aware of our plans and move toward turning things over to Simon.

Do you think it's ok to go ahead with a little more discussion on this point?

DR. DWORKIN: Sure, but maybe my two-cents worth would be to turn it over to Simon at 1:10, because we really want to make sure he has enough time to discuss the manuscript that he's going to be leading.

DR. KERNS: Yes.

Alright. So I'll call on several people in quick succession and try to wrap up by 10:10; I mean 10 after the hour. I'm going to call on Isabel Jordan or Christine Chambers, who had comments, and then Lee Simon, and then go back to my list.

MS. JORDAN: I think one of the fundamental tensions that people feel is that when you're bringing in patient partners to do work, especially if it's new for you, fundamentally, we're coming from often a very different perspective, especially

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if you're bringing people in that don't come from an academic background or a background that involves coming from a post-secondary institution. And that can be fundamentally uncomfortable because you might hear things that you haven't heard before and opinions that feel very discordant to your own. And that's fundamentally uncomfortable, and that's ok. It's ok to be uncomfortable, and it's ok to have awkward conversations.

I really echo the previous comments that increasing your facilitation skills is really important. But I think one of the most practical tips to have, and I think one of the things that has, from a personal point of view, made me most comfortable is if from the beginning there's clarity really made around whose role is in charge of what.

So what are you actually asking the patient partner to do? What do you want them to chime in on and what don't you want them to chime in on? What is the actual purview of this project or this clinical trial that they can have some agency

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around so that they don't go down the road thinking that they have agency over something when they don't?

The parts that you really have said that you want them to have some agency over, you listen to them, and you take in their opinions, and that they know where the limitations are from a regulatory point of view that you have no control over, and those continuing clarifying conversations that may be uncomfortable kind of keep happening.

That tension around not agreeing over things is ok as long as you keep having those clarifying conversations. I don't expect to have birthday cake every day, even though I would really like to. Nobody wants everything to go their way all the time. They understand they're working within the team. But you don't want the bait and switch either, where you think that you have control over something because it's not made clear, and then you don't. So that's my two cents of advice.

DR. KERNS: Alright. I noticed Christine basically was giving the handoff to Isabel, and

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she's been mostly shaking her head and smiling as Isabel was -- so I don't think I need to call on her.

I'm going to actually call on Lee Simon, who put something in the chat about OMERACT. Would you like to make your comment, Lee?

DR. SIMON: Yes. Thanks, Bob.

We work in OMERACT as if there is literally no difference between our patient research partners and our investigators and other individuals who are stakeholders, and we often have regulatory people within our discussions.

One perfect example was when we were developing the criteria for measurement of domains of flare of rheumatoid arthritis, and pain is a very important part of that. But there was a big debate about fatigue and how much fatigue plays a role; and how much of it is driven by pain and all the various different components; and whether or not that would be 1 of 7 things to measure; and how would you measure fatigue.

Interestingly enough, this actually evolved

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into a rather closed meeting at the FDA between the review divisions, the senior leadership, OMERACT, and patients as they were discussing the issue of fatigue because the critical path was developing an actual format and approach to fatigue.

The way it actually got resolved over some time -- maybe even six months -- was recurrent delphi of a larger group of people that were not necessarily only those involved in the discussions at the table; that in fact it then led to a real congruency of thinking regarding what we were trying to achieve.

I think that the reality is you have to assume, and everybody has to assume, that everybody's equal around that table. In my field, physicians believe that they're the ones that are the adjudicators and can know how a patient responds. What I've learned, both by being a regulator and clinical investigator, is, in fact, it's the patient who knows what's going on. We think we observe what's going on, but as physicians, we really cannot understand entirely.

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So I would urge anyone that has that kind of conflict that Mark has brought up, which is real and can happen, is that, fundamentally, you work it out. You continue to talk, you continue to debate, and you go to a larger audience and decide on how they think about that and how to do that. So that's what I want to point out.

DR. KERNS: Thank you, Lee, very much.

We have just a couple more minutes, and there's a lot going on in the chat. Because Lynn Laidlaw doesn't have the capacity to speak orally, could I ask Chris, would you prepare a quick summary of what Lynn has said, to speak orally, in just a minute?

Let me, in the meantime, call on Kathryn Martin, who's been very patient, to make your comment, and then I'll close out this by asking Penney Cowan to make a comment. Then I noticed Kristin Carman's hand just came up, but I think after the first two comments, we'll have to go to Simon.

So, Kathryn?

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DR. MARTIN: Yes. Sure. I just wanted to say that Lynn and I actually have been part of a team supervising two medical students undertaking a review, looking at and trying to evaluate the reporting of patient partner involvement in chronic pain research. Very interestingly, part of that conversation around how is that being reported in the literature and the role of the editors and journals for this is quite interesting.

The few number of papers that we've been able to identify that do it well, and the areas in which they bring this into their manuscripts and where things are actually highlighted, we were even looking at getting things like patient partners being included as authors and whether they had been acknowledged.

It's still being worked on at the moment, but I do want to say that we have been looking to see how -- because the focus was how patient partner involvement has been involved across all the different life cycles of research. So yes, it's quite interesting, actually.

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So I do think that there is hope to try and improve that in terms of reporting, whether or not that's through some of the reporting tools like CAS [ph] and other stroke [indiscernible] guidelines, et cetera, trying to make sure that patient partner involvement is noted there. That could be another avenue as well.

DR. KERNS: Thank you very much.

It is 1:10, but I'm going to ask Penney to make a brief comment, and then I'll turn things over to Simon.

MS. COWAN: I think one of the problems is that -- and someone said this earlier -- we're representing our own opinion, and we can't speak for everyone else. So when we have those kind of opinions, it's our word, so it may not be taken -- I always feel like we need to ask [inaudible – audio gap] -- goes down to whether surveys or focus groups -- [inaudible}, and those that are underreached, as we heard before, and ask them to chime in, and then let's take that back along with the opinions.

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So it just gives more validation, which I think all people are looking for that validation. So it might be better to get a broader view if there is that disagreement on what do others think.

I know, Sean, we did do one [inaudible} on some of those issues because we wanted to know -- it wasn't on this particular one, but I think that's something that he had delved into, and I think it's important [inaudible] both, focus groups, but also surveys. The problem with a lot of this is people who access all this information are not your average consumers because they have all the access, and like Chris said earlier, they're more educated people.

So I think we have to actually go out on the ground; I mean, that's what I've always done. I always believe in the underdog, and let's go out and meet them where they live. Whether it's a VA or an Indian reservation, it doesn't matter; in a farming community. That's where we need to really start talking to people, and I think we've always missed that.

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DR. KERNS: So, thank you very much Penney.

Thank you very much to our presenters today, and to this rich discussion. It's very clear to me that Simon has his hands full managing the chat and the dialogue that we're going to undertake now. It's just been great. But it also seems clear that we've kind of transitioned into a broader array of issues and just reacting to our panelists today.

So again, thanks to the panelists, and at this point, I'm going to hand things over to Simon.

Discussion and Development of Recommendations for Publication

DR. HAROUTOUNIAN: Thanks so much, Bob.

First of all, I tremendously enjoyed those last three days of conversations. I learned a lot. I have to admit that even though it might be a somewhat challenging test to try to incorporate all the comments and viewpoints in a recommendation manuscript, I'm really very excited for this opportunity to try to do it.

I really wanted to start with presenting to you some thoughts on how we might want to structure

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this manuscript going forward. But I think as we would do around the table when we have different partners -- for example, thinking about a design or clinical trial -- I really want this to be a discussion where everyone feels equal to contribute and to share ideas, and thoughts, and criticize things that might not look appropriate.

So I will take the liberty to present some initial thoughts about the management structure and highlight some key points where we might want to have a discussion and some clarifications. But then I think we'll have ample time to allow both for specific comments about the manuscript, but also some thoughts about previous presentations, where people didn't have a chance to share their views.

The overall thought process about the proposed IMMPACT XXV manuscript, the initial idea was should patients be included as partners in trials of pain treatments? And I think based on the presentations that we heard in the past three days, the answer to the first question really

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seemed to be quite obvious; that there is really a strong rationale for including patients as partners in our clinical pain studies and trials, whether it's drugs, or device, or anything else.

I think one of the key points that we'll need to present as a part of this manuscript is really try to highlight some of the key benefits that are related to including patients as partners. I think we had several very important and thorough presentations of what would those benefits be, whether it's related to retention and recruitment for patients or whether it's related to the fact that the studies are going to be more clinically relevant, and I have some of those details on the next slide.

One of the thoughts was, actually, as we're going to present this to the readers, also be transparent about what might be the costs associated with engaging patients as partners in the continuum of the clinical trial design and conduct. And I'm not talking just specifically about monetary costs, but also indirect costs that

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several of the studies or several of the manuscripts have highlighted.

One of the ways I would propose for us to think about the benefits and the costs is rather to present this as value. So what is the value of having patients engaged as partners in clinical trials, and really thinking whether those benefits outweigh the potential costs, and what are the different issues associated with those costs, and whether there are ways to overcome them.

I think, based on that initial presentation, the idea would be to describe if we're going to include and involve patients as partners in our clinical research and how to do this well. I think we have heard several presentations about what are the different components that need to be considered and what are the different lessons that we have learned from different areas -- and maybe not necessarily pain specific -- that we can maybe translate, adapt, or extrapolate it to come up with some certain recommendations about advice in clinical pain treatment studies.

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It would also be important to think about what were the different gaps that were identified in this process so we can both come with our best current recommendations for the field, but also highlight some of the key gaps and formulate potentially as future research agenda items. And maybe the manuscript that will result from this meeting would actually have some of those future agenda items where researchers, and regulators, and funders can perhaps take, as we would hope those items might have some kind of impact.

So to initiate the discussion -- it's hard for me to monitor the chatbox, so Bob or Chris, if you could help me, perhaps, monitor it, and if there are any particular urgent comments, maybe to let me know -- one of the points that I thought would be useful to start with is some summary based on the initial presentations, but also the narrative review that was presented on day 1 of representative items that were collected about the perceived benefits that we might want to outline in our manuscript, and also some of those challenges

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and costs.

Some of those items that can start this conversation, among the benefits that were presented in those three days, really are things that improve relevance of research to patients and patients priorities. In many different areas, there were points raised about the significant contribution to trial design. Lee Simon presented the issue of fatigue or thinking about the outcomes that really matter to patients; improve patient information materials and informed consent documents.

We heard that language matters and we want to make this about the patients rather than other team members; improve both enrollment and retention, including decreased attrition from the studies, and really important points about improve dissemination, as well as further down the road, implementation of research findings, and potentially really increase public trust in the research process and outcomes, as patients are key partners in this process.

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Some of the key challenges that were raised really are related to time as a cost component both to researchers and patients and patient partners; potentially increased cost; and the fear of symbolism, or tokenism, or a checkbox issue, including patients as partners in a non-meaningful way.

I think, as Sean Mackey raised, the component of what do we do if there are some changes to research scope, for example, that are not feasible in terms of regulators and how to address some of those conflict resolution issues.

As well, I think one important point is that oftentimes clinical researchers are not necessarily trained in this component of engaging patients as partners, and how do we address that lack of resources and lack of training? I have another slide at the end about the potential resources and what the recommendations might be for funders.

So I would like to pause here and really hear from the group, both in terms of the general structure or the outline of the manuscript; whether

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this is something that sounds reasonable; whether there's criticism; whether there are key components that we can add; and also start the discussion with outlining the perceived benefits, as well as costs, or barriers, or limitations before we move forward.

I see a hand raised; Ian Gilron?

DR. GILRON: Yes. Thanks, Simon. Can you hear me?

DR. HAROUTOUNIAN: Yes.

DR. GILRON: I think this is an excellent way to organize things, and I really like it. I don't know how to layer this onto it, but I wonder if also we can add the different domains in which patient partnership can occur. For example, very literally and directly to help inform study design and conduct versus patient partners being involved in setting research priorities and getting involved in research policy, to even another level of having patient partners involved in governance of research organizations and research networks.

Your rubric will be very useful, but it may look different, depending on those different

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domains. So I'll just add that at this point.

DR. HAROUTOUNIAN: It's really good -- I do have a slide, later, that thinks about how do we present actually those costs, and values, and opportunities from the different perspectives. How can we consider the lens of, A, the researchers, funders, patients, but also, as you said, in the different settings?

In a phase 1 trial, things might look a little bit different versus a phase 3 trial, and how this manuscript can potentially address this plethora of complex -- I definitely don't have an answer, but I think it's an important point maybe to hear from others on the call on what might be the different ideas or ways of thinking about those different reasons.

DR. GILRON: I just want to add one last thing to that. In some discussions that I've had with colleagues from basic science, it seems that everyone at this meeting, we're sort of preaching to the choir, and we're all in favor of this and think it needs to move forward. But people in

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basic science, as one can imagine, can sometimes have challenges in trying to demonstrate the benefit tomorrow to the patient suffering from pain, when we're trying to understand fundamental mechanisms of nociception and how pain is transmitted, and getting into nuances of neural mechanisms.

So I think in terms of perceived threats of patient engagement, I think there is something that needs to be considered from the basic science perspective, where it would be hard to articulate short -- the obvious thing is identifying a new molecule that's going to treat pain, but understanding fundamental science of pain is hard to demonstrate the benefit to a patient partner. So that's another issue of perceived threats.

DR. HAROUTOUNIAN: That's a really good point.

Chris?

MS. VEASLEY: Yes. I was just going to say -- in response to Ian's comments, which are really important -- I can envision maybe two tables

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or diagrams, one which is similar to what David presented earlier today, which shows across the research life cycle or continuum, all the way from preclinical to phase 3 and phase 4 trials, the ways in which patients/stakeholders can contribute to different parts.

Obviously, the contribution at a preclinical space is going to be different than versus a phase 3 type of trial. Also, PCORI has some really nice rubrics, and others as well, that present, as you mentioned, all the different ways in which patients can contribute, all the way from unidirectional and focus groups surveys, all the way through being co-PIs on a study and having complete decision-making power on the grant. Those kind of rubrics and figures already exist.

Would that address your concerns, Ian, in terms of including those in the manuscript?

DR. GILRON: Yes. That's great.

DR. HAROUTOUNIAN: Yes, great comment, Chris.

I see that Christine Chambers has her hand

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up.

DR. CHAMBERS: Thanks for organizing this so nicely. I think it's fantastic. A couple of reactions and, again, I'm not sure if this is the place or not the place. But in particular, thinking about Ian's comment just now, I think we have an opportunity to shout out the importance of engaging trainees and that training component.

I think the basic scientists that we've trained through the North American Pain School, the patient engagement component there has been highly influential, and I think it has really influenced their thoughts on this moving forward. But I agree, when you have scientists who are more senior or very used to doing things a certain way, that can be a challenge. So I'm not sure where that training piece and opportunities -- but I feel like these manuscripts are so influential, so highly read, so highly cited, a bit of a call-out to training opportunities.

I also wanted to pick up on a point in the chat. And Bob, I see your comment. I can tell

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it's stressing you out, that all this dialogue is happening in the chat. And I think you just need to embrace it as like a parallel stream of engagement at the meeting, and we can download it after, and you can keep a record of it.

But I think this is one of the things I've learned, that some people and patient partners are just maybe more comfortable pasting in the chat. I think we have to acknowledge that sometimes we can be a scary group, and that could inhibit participation.

DR. KERNS: Christine, let me make a comment. I entirely agree, except for one thing, which is there are a few people that are on phone only --

DR. CHAMBERS: Right.

DR. KERNS: -- and don't have the privilege of seeing what's in the chat, which is why I really -- I agree. It's not a black or white thing, but I do want people to feel encouraged to share orally if they're comfortable doing it.

DR. CHAMBERS: Sure. No, that's great. And

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sometimes with some of these meetings, they actually download the transcript and share the transcript from the Zoom chat after, so that people can see what happened in the chat.

But I think this issue around the IRBs -- or in Canada we call them research ethics boards -- is really interesting. And I apologize if this came up; I sometimes have a hard time fully attending the Zoom meetings continuously. But this has been a very significant barrier with my own research ethics board not understanding patient partnership, wanting me to create consent forms for the patient partners who are collaborating on the project.

So I just wanted to flag that. I think that's something important that I didn't hear emphasized. And again, I apologize if I missed it. But that has been a significant barrier, and I think providing some commentary in the paper around how to best navigate and some of the challenges there might be helpful.

DR. HAROUTOUNIAN: Christine, thanks so much for this important point.

Can I unshared my slides as we're talking? I think it creates a little bit better vision of who is on the call, and we can at least see the faces. And then if I need to share something, I'll reshare them.

I don't think we really touched upon the IRB at all. We might need to go back and see what is out there in terms of published information and data as an additional barrier, and maybe consider that as another piece.

I see Jan Vollert has his hand up. Go ahead, Jan.

(No response.)

DR. HAROUTOUNIAN: You're still on mute; the sentence of the year, right?

(Laughter.)

DR. VOLLERT: I want to link into Ian's comment and Chris' reaction to it, which I completely agree on, and just want to echo it. We may even think that along the pipeline, patient engagement could almost be seen as a gradient, getting more and more important and more and more

impactful as close as we get to the clinic; so starting with basic research, where we would say patient involvement is important, but the scope and impact might be way more limited than it is towards the end in humans when we're going to clinic. And that is almost like a triangle shape going from basic discovery research into clinic.

DR. HAROUTOUNIAN: Yes. I agree. Thanks, Jan.

Christine Goertz?

(No response.)

DR. HAROUTOUNIAN: We can't hear you, unfortunately. You don't seem to be on mute, but -- sorry. We'll come back to you.

I did want to come back to one of the comments particularly about training. It is important, and we actually did have a slide. So while Christine is reconnecting, maybe I'll share one of those slides that Chris presented earlier.

Some of this relates to maybe some advice or recommendations towards funders, because I think one of the issues that came up is that oftentimes

we want to engage patients as partners as early as possible in the planning stages of the studies, rather than after the study has been funded, and many of the institutions and organizations don't have resources to potentially initiate that process early on. This might be even more important for communities with not a lot of resources or developing countries, for example.

One of the potential outputs from this meeting could be potential thoughts about what are the recommendations for providing training at two programs where there is clinical research, graduate programs, et cetera, but also to the part of initial, maybe, institutional resources for study planning. And that's another point where I think your input and some thoughts would be very helpful.

So maybe while people are thinking about this, we can try to go back to Christine and see if your microphone works.

DR. GOERTZ: Are you able to hear me now?

DR. HAROUTOUNIAN: Yes. Perfect.

DR. GOERTZ: Oh, great. Thank you.

DR. HAROUTOUNIAN: And I'll stop sharing so we can see each other.

DR. GOERTZ: Terrific.

A great discussion, and just getting back to the issue of the IRB, which I think is really critically important, it's not just the IRB. There are so many ways in which the infrastructure upon which we build our research is not focused to consider patient engagement. From the IRB, all the way through the discussion that we had earlier about publications, I think that is a really important barrier that we need to address.

I also would like to comment on the discussion that we just had about basic science and what impact can patient engagement have on the continuum of research. And my question to all of us is, who gets to decide that? I mean, who decides whether patient engagement is important for a particular project? In the same way that investigators don't get to decide what is safe for patients, should investigators get to decide whether patient engagement is appropriate for a

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particular study? I just think it's something that we need to think about.

Finally, Bob, earlier you had said that one of your hopes for this meeting, and my hope also, is that this can serve as a catalyst for really facilitating patient engagement in pain research. I think that that's incredibly important. But I wonder, that we are a group of mostly researchers with some patients who are already pretty sophisticated when it comes to participating in research, and I'm just wondering if there's an opportunity, when we get our key points put together, can we have some vehicle for getting public comment, broader public comment, and maybe including that as part of the manuscript, or including that as an addendum to the manuscript, so that we really make sure that we're not participating in some group think that is somehow missing really important points. Thank you.

DR. HAROUTOUNIAN: This is fascinating and I think challenging -- no, not challenging, but I think it's a really interesting proposal. I don't

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remember that any of the IMMPACT manuscripts had this sort of mechanism of public comments.

But, Bob, Dennis, maybe this is timely and interesting enough, and maybe in communication with journal editors something to think about, that if this is patient-focused output, do we actually want maybe broader representation of thoughts of patients on the product of this meeting?

DR. DWORKIN: I'll respond to that. There are, of course, preprint kind of websites for manuscripts; MetaArchive, et cetera. I actually don't know the policies of Journal of Pain and Pain with respect to putting a manuscript on one of those sites.

DR. JENSEN: You can do it.

DR. DWORKIN: Okay. That would be a way to solicit public input that could then be included as an electronics supplement when the manuscript finally gets submitted to Journal of Pain or Pain. So it's certainly something that we could do. We've never done that before. It's kind of cool, so maybe we should think about how that would work.

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Just one question I would have is, I don't know how many people are able to find manuscripts on places like MetaArchive. So how do we let the broader public, patient stakeholder community know that a manuscript is available for review on one of those sites? I would have to be educated about the answer to that question.

DR. HAROUTOUNIAN: Maybe we can leverage, really, the infrastructure and people who are in this meeting, whether it's resources that PCORI may have, or some of the patient organizations, or patient advocates may have, or the Maryland group may have. I think there are probably some opportunities for outreach to solicit some response. But again, I do agree with Bob, with the point of how do we get, actually, to broader representation since people are not going to log into MetaArchive and find that IMMPACT manuscript and voluntarily respond to it?

DR. KERNS: If I may make one additional comment on that point. I do want to bring up the issue of the digital divide, in that there are many

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disadvantaged -- in fact, I think we're becoming clearer about social determinants of pain and chronic pain, and some of the most disadvantaged people are at the highest risk.

So if we are going to take that kind of step, I do think we have to think about how do we reach those people that don't have internet access, for example. Thank you.

DR. HAROUTOUNIAN: A very good point.

Alright. Thanks so much. McKenzie had her hand up.

DR. FERGUSON: I was just going to put a comment in the chat, and I think Chris has spoken to this earlier, about the value in clarifying the roles of the patient partners across the whole pain research continuum. Maybe by doing that, we can really show the researchers that it can be a scalable approach. I think it seems a little overwhelming to think about all the roles that PPIs can have, so maybe by delineating that at each point in the process, it can be somewhat manageable for researchers.

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Also within that, I really like the idea of then going back to patients and saying what would be the priority within these roles that you think you can add in terms of where we should be focusing our efforts if we can't take on the whole approach.

DR. HAROUTOUNIAN: If anyone has particular feedback or thoughts on McKenzie's point?

(No response.)

DR. HAROUTOUNIAN: I was wondering how we can address that in a manuscript, in a sense that would it be a part of, for example, a table? If we're talking about the life cycle of translational research, then maybe the same way, we would have some sort of a figure with increasing roles or an increasing patient engagement component, I guess, based on availability, or training, or resources, and investigators could potentially implement.

I guess a little patient engagement is better than no patient engagement, and strong and meaningful engagement is better than a little. How can we potentially frame it?

DR. FERGUSON: I guess I'm a figurative

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person, so I envision a figure where you kind of have pre-trial main stage and post-trial rules of engagement; then within that, very actionable items where the patient partners can play a role on the team. Then just by visually laying that out, the researchers then can say, "Well, I can afford to do this, and strategically this is where I'm at in the continuum with my project now; or in future design, maybe I need to back up and consider pretrial because I wasn't able to do that now."

DR. FARRAR: Simon, this is John Farrar. I had my hand up, and it ties right into what McKenzie is saying; so if you're looking for additional comment.

DR. HAROUTOUNIAN: Yes.

DR. FARRAR: What I had in my mind's eye was more or less a table, McKenzie, which would say here are the things that you need to do in any clinical trial and here are the contributions that can be made by getting a patient partner or stakeholder involvement. In talking about how it gets published, that might end up being a

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supplemental table because it could be very long. But I don't worry about people feeling overwhelmed by that. I think the point is that they would, hopefully, read down it and decide what they need and what they don't need.

The point I wanted to make just before your comment is, as somebody who teaches about how to do clinical trials, a huge component of that, the biggest deficit to all clinical trials, is recruitment and enrollment. And it's very clear, in the studies I've been involved in with active patient partners, that they have a tremendous role in helping us understand how to approach the patient population we're interested in and getting them excited about participating and being involved in what we do.

So as a thought that I haven't really had from this particular conference, I'm teaching a course next semester in clinical trials, and one of the things I would very much like to have is a table to show the students and say, "Here's where your biostatistician works. Here's where your

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epidemiologist works. Here's where the geneticist works, and this is what your patient partners can contribute. And they can contribute, probably, to all or many of the different components, providing a different perspective."

So that's just from the perspective of the design of the clinical trial, the early part, and then obviously it carries through to during the conduct of the trial. I've never been on a trial that didn't run into real problems as it was starting, and the patient partners can contribute, and have contributed, very substantially to that.

Then thinking about how the paper gets written and what the important features of the outcomes we get that they need to be part of. Then, as we've talked about here, disseminating that information and getting it out there so that it gets applied. It seems to me that if we talk about it from the same perspective as the other important members of the team, it makes it much more real and much more direct.

Simon, what I'm encouraging is that we make

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the point that -- I'm old enough. I remember when statisticians were not considered an important part of the randomized-controlled trial, and now you can't write one without a statistician. I think that applies to our patients.

DR. HAROUTOUNIAN: Right. I agree. And it's both ends. It's both the training initially, but also I think Mark and Frank highlighted in terms of journals, if you have a mandatory or recommended component that's describing the patient-partner involvement, it sort of sets the stage that this is something that is expected to do, or this is the practice.

Christine I think mentioned yesterday that a part of this component, the training in the North American Pain School, it has become almost an integral part of teaching about clinical studies and clinical trials, and I think in most training programs, this is not a thing. You think about outcomes development, primary outcome measure, and randomization blinding, but patient engagement as partners, it's not something that is taught. I

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think as we're aiming for an impact for this manuscript, I think this is definitely a component that is worth discussing and bringing some examples on how this can be done.

I know that Mark Jensen's hand was up, so maybe, Mark, you can address it from a general perspective as well, but also hit other comments.

DR. JENSEN: I'm going back to the table because I'm really resonating with this idea that Jan raised, that the amount of involvement might increase as we go from early basic to phase 1, phase 2, and phase 3. And these papers, these IMMPACT papers, are very impactful, and in my view are impactful to the extent that they make strong recommendations that say, "You know what? Do this."

So if we can get to a point where we can say, "You know, you really need to do this," I'm envisioning a paper where it goes from basic science, through different phases, and then a column that says, "You know, we think that for each of these phases, you really have to do this. This

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is just critical for us moving forward," and just drawing a line in the sand. Then maybe a third column says, "You know, this would be a good idea," and we think it'd be good.

But I think that could give the reader real clear guidance, and that would also help us editors go, "You know what? If there's a consensus that this column is real critical at this phase, then we could say to our authors, 'If you're submitting a paper at that phase, you ought to do this.'" So rather than a blanket checkbox of why didn't you do this, kind of what Bob was talking about before, making it more nuanced and specific to the type of study that's being considered.

DR. HAROUTOUNIAN: Yes. Wonderful. This is very helpful.

I have Isabel Jordan next, and then Bob Dworkin.

MS. JORDAN: Hi. I just wanted to go back to -- I can't remember who it was; it was a little while ago -- talking about that we all kind of said the people that are here are already quite

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privileged in that we all have bank accounts. This system is set up for us, and there are barriers for patients to participate in any kind of research endeavor as a patient partner.

A lot of us look at engaging with patient partners as, well, of course, we can send them a check, or electronic funds transfer, or we can send them an email. This is true from working with a research team, to working at an institute, or communicating with a journal.

I think it's really important to think about who's making these decisions about how these systems work and who we're leaving out of these decisions about how this works, and how we can overcome this. I think it's really important to think about, even with journals and doing reviews, are we engaging with patient partners to inform our actual engagement work? So not just a patient partner with lived experience on a project, but are there patient partners, people with lived experience, that are actively working with us on how to engage, looking at the process of engagement

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so that we're not leaving people out just by the systems that we have.

I think it's a huge barrier that leaves people out throughout the entire process, without many of us even noticing that we're doing that. I think it's monumental. And it doesn't matter whether it's in pain and clinical trials, in this case, engagement is engagement, and it's a barrier everywhere.

I think it'd be really important to talk about this in the how tos because it's the responsibility of the researcher when you're engaging with folks to understand what those barriers are, and sometimes the only way you can do that is if you've already talked to somebody who has some understanding of that.

DR. HAROUTOUNIAN: That's a very important point, Isabel, and also thinking not only about global resource, for example settings, but also geographically across the globe, I think some of those recommendations that we make, we need to be very thoughtful that they are applicable not just

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in Europe, United States, and Canada, but rather high-quality research conducted elsewhere. And we need to be thinking about those things that are applicable for a different setting [indiscernible]. Thank you.

Bob Dworkin?

DR. DWORKIN: I think I'm about to disagree with a bunch of people. When we first started thinking about this meeting, probably a year ago, the focus was going to be on patient engagement in clinical trials. And then at some point, I think about three or four months, maybe five months ago, it was extended to clinical pain research.

We've done no preparation whatsoever about patient engagement in basic science. Allan Basbaum has been in this meeting, partly. Jim Eisenach has been in the meeting for the last few days, but we haven't asked them what they think about patient engagement and basic research. We haven't had a systematic review. We haven't invited any basic scientists. Jim and Allan are here because they are members of ACTTION's steering committee.

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So there's been zero preparation to, actually in any meaningful thoughtful way, consider the role of patients in basic science research. And I would make the same argument about phase 1. Phase 1 studies are a whole different animal. So personally, I have zero expertise in phase 1 studies with pharmacokinetics and, obviously, know nothing about it. I don't even get to say anything about it as far as I'm concerned.

So, I actually would suggest that to make Simon's life easier, because he has a life outside of preparing this draft manuscript, that we keep the focus on patient engagement in clinical pain research and try not to tackle things that we are not prepared to tackle, because we haven't invited the right people to the meeting.

So that's my two-cents worth. I know Simon has a family and a career, and if we broaden this manuscript to a monograph or a book, he's not going to see his wife and kids for the next year and a half.

DR. HAROUTOUNIAN: I appreciate the

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sentiment, Bob, but I think we should probably keep the focus on what's going to be a high-impact output from this meeting. But you have a perfectly valid point in terms of just our preparation for the meeting, because this is a topic that can be done -- if this component of the manuscript is going to be done outside this meeting, going back to the literature and identifying things, this can be prepared as maybe a separate project where people would volunteer.

I see that there are some comments in the chatbox about limiting the scope.

Lynn?

MS. LAIDLAW: Sorry. I missed a lot [inaudible – audio gap]. My WiFi was terrible. As I'm thinking about a publication and whatever, I always come back to what really matters. I think what we heard over the past couple of days is that it was values that mattered. I would hate to see that we are putting forward patient engagement or patient public involvement as an asset when it's not, when it's driven by values, and you can work

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out how to do it. But the most important thing is coming at it with the right values, and then you maybe don't do the harm that Isabel talks about and that I have experienced as well. There's a saying in co-production that co-production is a state of being, not a state of doing. So you've got to be in the right state of being first, and then you do.

I just wanted to say a bit about evaluation, and just the essential tension and these productive tensions between something that I think is based on rights -- well, came out of rights -- that has been recertified. I don't know any patient partners that get involved to be evaluated. And what are you evaluating? Are you evaluating the difference you let me make or the difference I could have made if I had some power over my involvement?

I'm doing a bit of research at the moment as a patient researcher, as a patient partner. How do I evaluate the impact that has had on me as a person, which has been absolutely profound? How do you evaluate that? How do you evaluate the impact

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that patient public involvement can have on people?

It's all bound up in it. So I understand why you want to evaluate, but maybe we just need to keep in mind that, actually, you can't always measure what's really important. And the patient partner, it's maybe not like other things in research, and maybe we just have to accept that we can't evaluate all of it. And sometimes we need to stop to say, "You know what? This is good, and we think it's good, and we don't have to justify that."

DR. HAROUTOUNIAN: Thank you, Lynn, for this comment. I think it's an interesting and intriguing point. I think some of us may be sort of Lord Kelvin followers in the sense that one of his favorite quotes is, "If you cannot measure something, you cannot improve it." And I wonder how do we -- as you said, can we agree that this is good and not necessarily go into the particular details? How do we agree that this is good? We might be a very biased group. I think it's really interesting to think about how do we assess and

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convince others that this is the right thing to do.

I was really interested in your point about how do we assess what happened to the patient partners who were involved in their own perspective. How did that affect? But I think it's almost a separate question from what we have for this meeting in a sense that it's thinking about how we improve the clinical trials. I don't know if other things, like whether the effect of participants' engagement on the patient partners need to be measured as a part of this particular endeavor. I think it's, separately, a really interesting and intriguing question.

MS. LAIDLAW: I'm not going to take up any more time, but there's a couple of really interesting papers that I'll put in the chat about the impact of patient and public involvement or the engagement on the researchers, which then has an effect on the research.

DR. HAROUTOUNIAN: Which is another question that is probably outside of the scope.

MS. LAIDLAW: And why isn't that as valid as

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some other metrics that we might -- I just really want to push back against this a bit.

MS. VEASLEY: I think that can be one really important recommendation. Maybe you missed a little bit of the discussion earlier. It was to identify the goals and what each of the stakeholders in the research group would consider success, and to measure all of that.

This meeting also hasn't talked about the need for multistakeholder groups. Sometimes you need primary care providers, or clinicians, payers, and all types of other stakeholders to be part of the research group. We all come to it with a different background and different perspective, and we all have different definitions of what success means.

But I agree with you that we can't measure everything. I think we need to state that. Not everything can be measured, but here are the types of things that we feel could be measured and would be impactful to measure; not just what is the impact of patient engagement on the science or

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research, but vice versa. Like you said, what's the impact of our engagement or other stakeholder engagement on the research team or other stakeholders? So I think that could be a really important recommendation.

DR. HAROUTOUNIAN: Thanks, Chris, for pointing this out. I think in terms of what success looks like, for the same team of investigators, for example, with patient partners and everyone -- for example, for the PI, publishing the paper in JAMA may be the point that is considered a success. If it's an industry trial, maybe getting a drug approved would be a success. From the patient partner perspective, getting something that can help the condition with less side effects, that is a success. And this will look completely different in how we prioritize which are more important to measure as a success of the program.

I think there's really a point about there are several things to measure. There are probably different ways to approach them. And we also need

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to realize that we may be unable to measure all of those things in any meaningful way. So I think it's probably lending to a nice paragraph that is addressing some of those points.

I think Jen has her hand up, and then Ian.

DR. GEWANDTER: Hi. Thanks. I guess I'm coming to this probably as one of the more naive people in the room because most of my patient engagement has been more on the qualitative interview, so more of the research way than in a partnering way. So I feel like I've learned a ton today, so thanks everybody for all of your thoughts.

So I guess as someone who would probably be a consumer of this manuscript, maybe more than an author, I think, for me, what would be really important -- because, to me, it's a lot less overwhelming, the idea of getting patients' input or people with lived experience input on a particular specific study idea I have. And what's more overwhelming and scary to me, kind of as Isabel pointed out, is this concept of trying to

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establish these long-lasting relationships, and how to do that, and what do I bring to the communities to make them want to engage with me, especially underserved communities as like a middle-aged, white lady.

I think maybe not like a detailed how to, but at least some references, two examples, of how that's been done well like -- sorry, I forgot her name -- the person who talks about their work in Maryland. Those kinds of things I think would be really helpful for me as someone who is reading this manuscript.

DR. HAROUTOUNIAN: No. Thanks so much.

Maybe I can share the slides for a second. Some of the things that we heard -- and I think in the manuscript we should be addressing them maybe in an order -- is thinking about the process. Once we determined that it's important to engage patients and partners, I think we had a lot of material presented on thinking about how to identify, locate, and incorporate patients in the planning. We had quite a quite a bit of

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information there.

I think John's suggestions in the presentation on how to think about including diverse and hard-to-reach population partners in that group, that probably, I think, needs another component; incorporating patients in the conduct of the clinical study, as well as, eventually, dissemination and implementation.

I think maybe another point, really, Jen, that we could think about is how to maintain those partners and what might be the strategies to actually building the trust component. I think one thing that maybe we barely touched it because it wasn't presented formally, but maybe a little as a chat conversation, was involvement in the data analysis and interpretation component.

I think there were some views that maybe patients may not have as much to say, but I think actually that's going to the question of who decides where patients voices are important or not. I think there was actually quite a bit of input that patients should be involved in thinking at

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least about data analysis. Maybe they will not be running your regression in R, but in terms of providing valuable input on the metrics and how we interpret the data, it's also probably worth addressing along those specific recommendations.

I think we did discuss how to measure success, and Dr. Forsythe really brought this plethora of information, and then mentioned 35 to 40 different tools that may be existing out there for measuring at least some of the components. I guess the question is we don't envision -- or I'm not sure we can hope to come up with a specific tool for assessing success in specific domains, but at least providing some recommendations of what researchers may think about using and potentially implementing in particular settings. So thanks, Jen, for that point.

Back to Ian.

DR. GILRON: Yes. Thank you. My comment also has to do with measurement and also the fact that we're early on in this. I felt more urgency to make the comment when I heard Mark Jensen saying

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that this needs to be mandated now in articles, and people need to show that they've involved patient engagement.

I like that you have how to measure success. I wonder if we should change it to how to measure impact. And in particular, there are certain aspects that we don't need to measure that we know we appreciate inherently that this is an important thing to do and that we should be doing this, but we should be mindful of potential threats. I'll just give some simplistic examples, and they're not necessarily a concrete example, but they're just a way of illustrating some things.

For example, in a study where you want to do pharmacokinetics, and if you ask a patient partner, they say, "Do you really have to stick me for phlebotomy to do this test?" We just want to make sure that the science of what we're doing is not necessarily compromised, and there may be some challenging conversations with patient partners to sort of explain or defend certain things that are critical for science that may not be popular to

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patient partners.

Another example is, does a patient have to be blinded to their treatment allocation until the entire database is locked for a clinical trial? It would seem nice for them to know as soon as possible, but if they continue to be in touch with research personnel, there's potential for unblinding.

I just have some examples of potential threats, where patient partnership could potentially have an impact on scientific quality, and that's just something that we need to be aware of and to negotiate. But just put that as a placeholder in the manuscript, that we're going to follow this process as we go, and we may have to make some course correction along the way.

DR. HAROUTOUNIAN: A really good point. I think it does come back to the point that Sean Mackey brought about those potential conflicts and how to resolve them. I think some of the suggestions of being transparent up front and defining roles, the way that each partner has an

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[indiscernible]. And John Farrar mentioned that if you're a statistician, you have a particular role, and being transparent and clear in communication up front so that expectations are set about the decision-making processes. But also what Simon mentioned, considering that everyone is equal around the table in terms of how we think about out people's input, even though not everyone can have cake every day.

I think it's a really important point, and I think we'll have to address that in the manuscript in some way that these are potential roadblocks or costs, and here are some suggestions, based on the presentations that we heard, that researchers can think about in terms of overcoming them.

Ewan had his hand up.

DR. McNICOL: It's Ewan. I just had a couple of quick thoughts on the manuscript. Usually when we do this -- I think we're all kind of familiar, or most of us are familiar, with what the IMMPACT manuscripts look like after these meetings -- typically the way they finish up is

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that we have these universal recommendations for how we'd like to see things changed.

I think in this instance, the recommendations need to be based on the individual stakeholders, from a patient perspective, from a researcher perspective, from an industry perspective, et cetera, and the recommendations will vary based on who those stakeholders are.

Further to that, Jennifer mentioned that she was kind of new to this whole thing, and this broadly is in its infancy. I wonder if in our recommendations we can make short-term recommendations, or recommendations based on -- if you'll just start with what's the small thing I can do right now versus these loftier or long-term goals that we may factor into it.

So maybe we can divide it into either a continuum or short versus long-term, small versus big, because I think some investigators are just feeling a little bit overwhelmed engaging patients and where do we even start with this. It's easy enough to reach out to an organization, but it's

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much more challenging to reach out to an underserved population, for example, and where do you get the time, and the money, and the resources to help with that?

That was it. I was just piggybacking on to what Jennifer had mentioned earlier.

DR. HAROUTOUNIAN: Thanks, Ewan. I'd be really happy to hear what people's thoughts are on dividing the recommendations based on different stakeholders, whether it's regulators, funders, partners, and investigators.

Karen, I see your hand up.

MS. MORALES: Yes. I just wanted to reflect back on this concept of how do you bring participants into the process at the very beginning when you're planning. One of the things the PATIENTS program successfully was able to do was to partner from the program level as opposed to thinking about it from the specific project level. We brought participants in on our budget line at, literally, the PATIENTS Program budget. We actually utilized some of our unrestricted funds to

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be able to incorporate patients and community participation at the very top level. That was suggesting that we really appreciated and valued their input as to the direction in which our program was going; as to the types of projects that we would bring into our program and what we would go after and the type of funding we would go after.

They actually were part of designing how we would move forward, and our patient representation, our other community partners, and our other organizational partners have a voting. Their voting rights were greater than ours as an organization. So if the patient group or our community partners voted 7 to our 5 or our 6, then we went with whatever they suggested and recommended.

So that's how we move forward with being able to incorporate them at the very planning level because it's not just about planning the projects; it's about planning your strategy as well and how you're going to move forward as an organization.

DR. HAROUTOUNIAN: Yes. This is a really

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great point, Karen. Thanks for bringing it.

I'm wondering, as a part of our recommendations maybe to funders as stakeholders -- as you said, the University of Maryland may have been fortunate in the sense that you may have some unrestricted funds to start the conversation or initiate some outreach, but most funding programs don't have that piece of money, where it's take this money and spend two years of building those community partnerships.

Are there certain recommendations that we can make to maybe make new opportunities for funding, or new announcements that would be targeted specifically in the training component, but also building those partnerships and initiating programs? And again, I might not be aware that there might be several funding mechanisms for that already, but that's definitely not the commonplace, and I would assume most institutions don't have something in place already for researchers to tap in.

MS. VEASLEY: Simon, if you're asking --

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DR. HAROUTOUNIAN: Yes, I am.
MS. VEASLEY: -- I was just going to say one recommendation for funders is something the HEAL Initiative has done, and Rebecca talked about it before, is they've put out supplemental FOAs for engagement specifically. It was kind of an afterthought because it wasn't included in the first initial round of funding, but that's one potential recommendation.
There could be specific awards that go up from NIH, or funding agencies, to specifically support pre-engagement efforts. Another thing they could do is to build into the actual grant a stage for planning for community engagement and time. So maybe it adds another 6 months, or 9 months, or 12 months into the grant, but that could be one pre-planning phase before they launch into the study. I don't know what others think about that.
DR. HAROUTOUNIAN: That's a good point, and I agree. I think the HEAL Initiative, the additional supplemental FOA is for HEAL investigators, so people who are already funded by

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HEAL if I'm not mistaken. So it is, to some extent, and afterthought, but still nevertheless important.
DR. DWORKIN: HEAL, PCORI is very US-centric, and I would be in favor of a recommendation that was really international, which is that we would recommend that medical schools have available the kind of program that we heard about from Maryland and the kind of program that Jonathan Jackson has at MGH Harvard. I heard last night that Vanderbilt has a similar program, and there are medical schools all over the world.
So I would advocate for being less US-centric and more international, the recommendation.
Jen and John Markman, if you'd correct me if I'm wrong, but I'm pretty sure that we don't have here in Rochester the kind of programs that Karen's describing in Baltimore or that Jonathan Jackson described in Harvard. And I think it would be great to have something like that at our medical school, and with every medical school in the world,

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and I don't see why we can't have that as a recommendation.
DR. GEWANDTER: Our CTSI has some stuff, but I don't think it's as advanced as what Karen was describing. I think the other thing, a little bit for me -- we are an EPPIC-Net site, so I've been thinking a lot about trying to establish this myself for our pain group.
It's kind of important that we have relationships for our specific areas, too. For example, if we had like an interdepartmental pain research program at the university, if we could somehow support this effort, because you're not always engaging the same people as like a whole medical school.
So I think that's where the challenge is. Even though the CTSI has these community engagement studios and stuff like that, and may have some existing partners, it's not necessarily the right people for me. So I feel like I have to still maybe use them as a resource, but would have to make my own connections and my own relationships

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like an investigator. It's kind of how I'm starting to approach it and feel about it.
DR. DWORKIN: But if we had someone like Karen or Jonathan Jackson at the medical school, they would be able to help us do exactly that. I personally think every medical school should have Karen or Jonathan on the faculty.
DR. HAROUTOUNIAN: I see Karen wants to respond to that specifically.
MS. MORALES: Yes. I just wanted to say that's where your partnerships come in, because we have partnerships with Morgan and we have partnerships with Coppin. We have partnerships with other institutions who were not as versed in this when we first started it in 2013. So as we started to grow and we partnered with other organizations in the Baltimore area, they're coming on board.
There was a question yesterday that was asked were there other institutions, as far as universities, also taking this up as an uptake in patient engagement. And I did say yes, I do see

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that other institutions are now willing to partner and to utilize this patient engagement concept as a framework for how they move forward in their own research, and they're taking it to their students.

The PATIENTS Program is actually currently developing the PATIENTS Professor Academy, as Gail mentioned yesterday. We're in the very infancy, but we're raising funds. We've already had commitments from three different organizations to support us at the $100,000 level each.

So this thing is growing, and I do believe that if you were looking at your existing partners, your existing relationships, and bringing them into this new engagement paradigm, it may take some time, but, Jennifer, you'll definitely be able to. If you're partnering with other groups around you, I think you'll be able to move that needle in being able to get into the communities.

DR. HAROUTOUNIAN: Thanks so much, Karen.

Isabel?

MS. JORDAN: It's really great comments on the need for training, specifically for engagement.

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It's really important. I think it's also important to recognize that if people are going to require patient engagement on projects, that funders specifically fund that engagement. If done well, we talk about that risk of trauma, the risk that it could go wrong, then having people have the necessary budget, time, and funding for this, and then somebody actually needs to fund that budget piece. I think that's a really important recommendation, and it's beyond the side of desk operation.

DR. HAROUTOUNIAN: Yes, I agree.

Before we go back to this initial structure -- and I think the comments were extremely valuable. I think there's a lot of work to do, to sift through them and see what's the best approach to organizing them. I'm not sure where we're having a consensus on many of those points, but probably with your input on some of the initial versions of the manuscript, we might be able to focus and reach some consensus on some of those key points.

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We have a few minutes left, and I want to give an opportunity to anyone who hasn't had the chance to raise any points related to either the manuscript or comments on the presentations, either from today or earlier; that we may have a few minutes to address before wrap up.

Bob Kerns?

DR. KERNS: Yes. Forgive me if this has already been emphasized and I missed it. I've been concerned -- and a few of you have heard this -- about barriers in the context of, for example, NIH, or particularly NIH program announcements or RFAs, that are even explicitly encouraging engagement of patient partners or people with lived experience.

The timeline between the publication -- even a notice of intent, let alone the publication of the RFA or program announcement -- doesn't really adequately provide a feasible timeline unless you're embedded in an organization that already has an active patient engagement group and you can readily tap into them quickly.

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I do think that there's a fundamental challenge at the very beginning of trying to really engage people with lived experience, even identifying key questions, or alone, helping the design and methods.

My recent experience, by way of example, is the IMPOWR RFA that explicitly called for engagement of stakeholders, including people with lived experience. I think our group at Yale did a great job. We have a lot of partners. We have individual conversations and so forth, but the bottom line was it was the investigators that drove the train to the finish line and getting the application in. And now we have an opportunity to really more fully engage partners in a way that really wasn't available to us up front.

If that was already emphasized, I do think that it's a challenge, mostly for -- I mean, it's really our whole community, but I think it is sponsored. I see Laura shaking her head in particular, so maybe it's even true with PCORI.

DR. HAROUTOUNIAN: Yes. It does come back

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to Bob Dworkin's point of whether our recommendations can be either institute specific, or country specific, or more global. And I don't know whether UK or Canadian organizations also have these short timelines. It's something that might be worth looking into and maybe providing some sort of comparison.

But I think a general recommendation to allow enough time and potentially provide preliminary resources for meaningful engagement of individuals with a lived experience, that's almost an easier recommendation to make. The question is how to formulate it for it to have an impact.

DR. KERNS: Really, I think there are multiple issues here. Money and time; none of us want to extend the whole timeline of an idea to implementation, so that's obviously an issue. But I will also add that I think it speaks specifically to emerging areas of interest around special populations, subpopulations of people with pain or pain and comorbidities, like people with chronic pain in opioid-use disorder, for example, where you

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aren't likely to have the right mix of people already there when you start to develop here.

DR. HAROUTOUNIAN: I agree.

It looks like Laura Forsythe may have some comments to that.

DR. FORSYTHE: I was just going to say I was nodding, Bob. We hear a lot about that. I think it's a real challenge, and probably offline I'd be happy to talk with you about a couple of the things that PCORI has done to try, in part, to address that, and also invite the opportunity to hear more about what are some other ways to get at that. It's a legitimate challenge, I think, that has a variety of factors that affect timelines for things, too. So I would love to continue that conversation.

DR. HAROUTOUNIAN: Thank you.

I think one component that we maybe didn't address as thoroughly in those two days -- we talked about patient engagement and planning, conducting research, potentially, and dissemination and endurance [indiscernible], et cetera.

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I think the implementation piece was left out a little bit, or to some extent, particularly if there is research with some meaningful results and how do we embed that in the community, and then what's the role of different payers that are involved in that system in terms of how patient partners can help us build some of those bridges and facilitate some of those processes toward actual implementation of research findings in the community?

We touched upon that briefly, but if anyone has particular thoughts on either approaches or where we might want to look for a little bit more information on that, I think that could be useful, again, for the manuscript.

DR. KERNS: Just one comment from experience is our pain management collaboratory and the advantage of engaging a group of dedicated veterans and service members, who themselves are embedded in communities that are important targets for future advocacy and spreading the word, if not actually supporting implementation.

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So I think it may be that there are different -- I don't know how other people think about this; I guess we really haven't talked about it. Is there a need to even think about different groups of patient partners or partners with lived experience across a research life cycle continuum? I think it has been mentioned, but maybe to emphasize that point.

DR. HAROUTOUNIAN: And I'm sorry I haven't been able to follow the chat if there were some comments that we didn't address or missed.

DR. KERNS: Well, I think the bottom line is I've recommended that we're going to have -- there's a lot of rich information there and a lot of people reflecting on each other's comments. I think that's all great.

We have to capture this. I think it was Christine or somebody suggested that we'll -- I know we have the capacity to do that. Valorie yesterday captured the chat and fed it to the core group. So we can do that and potentially not burden people with a long, extensive chat document,

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but some collating or something that we can disseminate to the whole group; a lot of great resources, so thank you, everybody, for your contributions.

DR. HAROUTOUNIAN: As Bob Dworkin said, there's a lot of material to work with. It might take more than a day or two to try to summarize the responses and any resources, and come up with some sort of initial draft to get everyone's input on.

DR. KERNS: Well, we gave you till Monday at noon.

DR. HAROUTOUNIAN: Yes. I think it was Tuesday, but something in that range.

So thanks, everyone. I truly appreciate the input and your willingness and energy to provide really useful and thoughtful feedback, and I'll pass it to Bob or Dennis for final remarks.

Adjournment

DR. DWORKIN: Thanks, Simon.

On behalf of Dennis and me, I want to thank all of you for hanging in till the very end. Dennis and I always feel that our primary goal is

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to make sure these meetings end before happy hour, Eastern Standard Time, and I think we succeeded today, so that pleases us greatly.

Of course, we owe an enormous debt of gratitude to Chris Veasley and Bob Kerns for putting together an absolutely fantastic IMMPACT meeting. I think we all look forward to the day when these meetings will be in person in some hotel in the Washington DC area, but given that we're not there yet, this has been a terrific virtual meeting. And really, I think IMMPACT and ACTTION are going to use it as a touchstone in designing future meetings.

Of course, we all owe an equally enormous debt of gratitude to Valorie and Carlos because this wouldn't have happened without their help, from A to Z, and all the technical support, and the kind of stuff that's been going around the edges of this meeting before, during, and after.

Finally, in terms of thank yous, I want to thank Simon's wife and children for freeing up the hours that he is going to be devoting to bring this

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manuscript over the publication goal line. So on behalf of all of us, we will be sending something to Simon's family to acknowledge our deep gratitude to them for freeing up his time.

Dennis, have I left anything out? I just feel enormous gratitude to everybody, and I'm sure I left something out, Dennis. You're on mute, if you want to say something.

DR. TURK: You've done a fine job. Thank you, Bob, for bringing us together toward this end. The next steps are going to be, as this manuscript gets drafted up, it will be circulated. Everybody here who wants to be involved as an author will have opportunities to have input into that. So don't think that this is over when this meeting ends, but rather this is the end of the beginning of what you're going to be seeing.

We do encourage those of you that do become involved with commenting on the manuscript to do it in a timely fashion. Given the number of people who are potentially authors, it really is important that if you are interested and want to contribute,

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you should do it in a timely fashion. And we will encourage Simon to give you some kind of time frame to provide responses because we don't want this to take three years to be submitted.

So thank you, everyone. We look forward to your continuing participation. The conversation is not over, obviously.

DR. DWORKIN: And for those of you who missed it, Dennis was just referring to the end of the movie Casablanca, that this is the beginning of a long, beautiful friendship, not the end of an IMMPACT meeting. Thank you all very much, and have a great weekend.

MS. VEASLEY: Thank you, everyone.

(Whereupon, at 2:30 p.m., the meeting was adjourned.)

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