PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

METHODOLOGY WORKSHOP FOR PRIORITIZING SPECIFIC RESEARCH TOPICS

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P R O C E E D I N G S

[8:36 AM]

DR. WALLACE: Good morning, everyone. I apologize for interrupting your discussions. The buzz in the room has been rising pretty dramatically over the last 15 or 20 minutes and I think is a great segue into what we hope to accomplish today in terms of dialogue and exchange of ideas.

I'm Paul Wallace and I have the privilege of moderating today's workshop. I think you all know where you're at, but just in case you haven't figured that out, you're at the PCORI Methodology Workshop for Prioritizing Specific Research Topics.

There obviously are many of us here in the room, but I also wanted to particularly welcome folks who were joining us by webcast. We will be showing the entire day by webcast, except for lunch, of course, you can kind of do that on your own.

And so also because of that and because many of us know each other in the room but nobody

knows everybody, whenever you do have a chance to speak, it would be helpful if you could also identify yourself and your affiliation so that we can all understand each other's perspective and where we're coming from.

In terms of just a very brief introduction to the day, I think that we're all increasingly familiar with both the challenge, mission, and opportunity for PCORI. I think we're aware that PCORI was founded a couple years ago, it's a not-for-profit organization authorized by Congress. Its key mission is to fund research that will provide patients, their caregivers and clinicians with evidence-based information needed to make better informed healthcare decisions.

And I think we're all increasingly learning over the last year just how complex that task is. I think that we've also been, I think, struck by the quality of folks that PCORI has been able to attract to the task in terms of staff, in terms of the Board of Governors, in terms of the Methodology Committee, and also in terms of folks

that take time out of the rest of their day to come to meetings like this and to participate in the run up to this meeting to think with PCORI staff about how we can move through some of these processes.

I think as we've all been sensitized to for years, there's an opportunity for us to create better healthcare decisions. The how to do that is particularly problematic and where we're particularly focused on now is one of the real challenging pieces, to say where do we focus our efforts.

So, PCORI is showing leadership in not only thinking about how to do this in a general sense, but how to build on the initial work, which has largely been leveraging investigator-initiated ideas fitting into a research framework to complement that with areas that require specific prioritization and emphasis going forward.

And a lot of our discussion -- all of our discussion today will actually be thinking about how that second approach can complement and extend what's been accomplished so far in thinking

about research prioritization.

I wanted to recognize the folks that are in the room. We all have a chance to identify our tribe. Now, today is a particular opportunity, so there are different tribes. You can look at your lanyard and you can determine if you're the traditional PCORI tribe or if you're the blue sparkles or the pink sparkles, or perhaps there are others. There are a variety of other tribes that are here too. We have folks from the Board of Governors, we have folks from the Methodology Committee, we have investigators, we have PCORI staff, and importantly, we have patients and we have caregivers and we have families of patients.

And I think that what we're also going to learn through the day as we try and identify our constituency is that none of us have just one constituency, all of us are a part of multiple constituencies. We're reconciling those ambiguities all the time, but what we want to do today is thoughtfully and consciously and explicitly think about how do we best reconcile the

points of view in the room so that we can come up with a practical, workable strategy for how we can go forward with prioritization.

You do have some materials that have been shared with you. I would call your attention to the -- this is paper in case you haven't seen paper for a while, but there are some paper tools that will help guide you to who is here. I also would call your attention to the fact that there are bios provided, so when I have a chance to introduce people, I will refer you to their bio, but I won't typically go through the great depth of the bio.

There also will be some PowerPoint presentations. Those will be made available on the PCORI website going forward for your further sharing.

Just to give you a very quick view of the agenda today, the logic model for today is to set context up front, think a little bit about where we are currently with PCORI and think a little bit about the need and opportunities for a prioritization scheme. We'll have the opportunity

to hear from Gail Wilensky about her thoughts about where we are now and where we're going with PCORI in general, but also with this particular process. And then we'll follow that with thinking a little deeper about what do we know about prioritization. We'll have the chance to hear from some folks who have thought about this deeply for a long time in some paper and we'll also then have a chance to get a little bit deeper into the practicalities of this from examining the experience of people that have been working with the proposed scheme, some experts that have thought a lot about what the scheme needs to address, and where are we in terms of achieving that, and then finally we'll have an opportunity to broadly sample the feedback and questions and opinions from the folks in the room along with a panel of folks that, again, have been thinking a lot about this from a variety of different leadership roles.

So, it's an ambitious day, it's a pretty busy day, but also my job is to do the best that I can to try and keep us on schedule and particularly

to remind our speakers that their role is to prompt discussion from the audience and we want to preserve time so that the audience can share with us your questions, ideas, and feedback. So, we will hopefully be able to encourage a great deal of dialogue through the day.

So, moving into the very first part of the agenda, it's really my privilege to introduce Joe Selby, who will launch us into the initial portion of context setting.

I think -- it's sort of that paradox that Joe's actually -- his effectiveness in the job means that he needs less and less introduction as we go forward and so I will be brief and just say that Joe has certainly been here a year, you made your mark, as he made his mark in his past career at Kaiser-Permanente where I had the advantage of having him as a colleague.

Joe is a family physician, an epidemiologist, a health services researcher, and really, I think, among many things, a mentor to thinking about how we can move these processes

forward.

So, Joe, let me turn things over to you and you can help set the stage.

DR. SELBY: Thank you, Paul. Good morning, everyone. It would be a gross understatement to say that we are not excited -- to say that we are excited about the fact that this day has finally arrived. We've been looking forward to this day for I don't know how many months. This discussion of how PCORI is going to get some degree of specificity in its research agenda has been with us, has been with the Board, has been with the Methodology Committee, the growing staff, almost since day one.

And a lot of preparatory work has gone into this. No one has done more in preparing for today than Dr. Rachael Fleurence, who you all know, I think, and you'll hear a lot from, but all of you, all the guests, all of you who participated in the piloting of the prioritization process have really contributed a lot, and so we're excited to think through this day and, as Paul said, my job is

to set a little context, and that's all I'm going to do, just flesh out what I've just said, explain to you why, in fact, we are excited to be here today and really curious to see how the discussions and the deliberations go today.

So, who are we? And what are we striving to accomplish? Paul already said as much, almost as needs to be said about who we are, a new, brand new, relatively large, non-governmental, not-for-profit funding agency for research that aims to answer questions that patients and their caregivers and their clinicians face. So, we're not trying to understand what causes diseases; we are trying to provide research answers to common questions.

We hope that our research is the kind of research that will actually -- because it does address those questions, because it's true to the needs of patients and stakeholders and clinicians. We hope that it will change practice relatively rapidly.

If there's one hallmark to our research it would be that it's the kind of research that has

practical utility, changes practice rapidly. That's very self-serving for PCORI, in one sense, because in just five years we're going to be evaluated to see if we made a difference, so it's in our interest to fund research that makes a difference.

But, truthfully, it's in everybody's interest.

Second critical hallmark of PCORI-funded research, which hasn't been called out before, not to say that other funding agencies haven't attended to this to a lesser or greater degree, but in our mission statement crafted by the Board of Governors, Paul read to you a minute ago, down to the part about by producing and promoting high integrity, evidence-based information. He didn't read the last part, so I'll just fill that out, that comes from research guided by patients, caregivers, and the broader healthcare community.

So, that's part of what makes it relevant, we think, is that it will guided by those end users of our research.

We were charged in the legislation with saying out of all the possible research we could do, what research are we going to prioritize, and PCORI, last May, published its National Priorities for Research. They make a lot of sense.

The first one, the assessment of prevention, diagnosis, and treatment options, is probably what most of you expected PCORI would fund. Some people call this the CER priority among our five. I argue daily that all five of them are comparative effectiveness research, but this one certainly is that one that's focused at the individual patient making a decision about prevention, practice, diagnostic tests, or a treatment modality about which they have a choice, about their deliberating about whether to take that up.

The second one, though, and we think not much would be gained by adding to the evidence in priority one, not much would be gained if we don't improve the healthcare systems in which patients and their caregivers and their clinicians are

interacting to make these decisions. And I can't -- I don't think there's any theme that more people resonate with, as I go around and talk about PCORI, than the notion that our health systems, if we're receiving care within a system, they've got to be improved. Still a lot of people that there's just no way that you could say that they are within a system as they get their healthcare; it's so fragmented that there's just no recognizable system there yet.

So, number two, improving healthcare systems for all the things that I know you know systems can do when they're working well.

Number three, communication and dissemination research. This is not dissemination, per se, this is research on how we get information out given that we've got good research. How do we make it available? Through what channels? Through what organizations? And with attention to what patient populations and the particular needs of those populations? And having gotten the information out there, how do we support patients

and those they're working with, particularly their clinicians, in talking about the evidence and in making those decisions? So, that's priority number three.

Assessing disparities recognizes the fact that much comparative effectiveness research recognizes differences in response to treatment, differences in preferences, differences sometimes even in biological mechanisms and in cultural expectations, all of that is -- that actually is generated by comparative effectiveness research, but it helps to explain disparities. We turn it around and we say, we want to use this evidence to eliminate disparities. That's priority number four.

And number five is the infrastructure priority, funding for developing better methods, funding for developing better data infrastructure, and funding for training researchers, clinicians, and patients to participate in patient-centered outcomes research.

So, those are our five priorities. We, in

general, we intend to prioritize within these priority areas, so that's about as narrow as we've gotten to date and that's what we're here to talk about, getting to a greater level of specificity.

Okay, we have two approaches, and I hope you can see this, I'll kind of take it down for you. We have two approaches to getting to funding announcements and funded research. In the end, they both lead to high priority research, we would argue.

The first is one that we've already done. It's in place. We issue very broad funding announcements. You may have seen them. There's one associated with each of the five priorities. These invite good ideas regardless of the condition, regardless of the method, regardless of the study population. We say, simply, we're open for business, send us your best ideas in this priority area. We give some examples, but we say, by no means is this the scope of what we're interested in funding. Send us your best ideas.

We also let applicants know that they must

partner with patients, clinicians, and other stakeholders. So, everywhere in our research application says, we will not take research if this is simply sent in by a research shop and there's no connection to patients and the other end users of research. So, get together with patients, get together with other stakeholders, generate the research question.

Take a look at our review criteria -- and you'll see them today, but we have a set of review criteria, I've already mentioned they kind of emphasize mostly the likelihood of impact and the importance to patients of the research as well as, of course, rigorous research methods.

So, take a look at these review criteria, put your applications together, send them in, and we then convene peer review panels. The peer review panels have patients and stakeholders on the panels along with scientific reviewers, and they grade these applications according to our review criteria.

So that gets us, we think, to a high

priority set of applications across a broad range of topics, but a key thing is that we do feel in the end that these are high priority research questions that need to be addressed.

But this is what many people have called an investigator-initiated approach to funding research. We've actually, from time-to-time, been criticized because we haven't really gone that next step and said, we want research in this specific area because it's the highest priority, the most important.

We think this is a critically important approach to research. We don't think we'll ever capture all the good ideas in any prioritization process. We want to be open to research ideas that come from the community, that come from the research community, the patient/stakeholder communities.

So, we expect, I predict, that this will always be one of the ways by which PCORI funds research. Exactly what proportion of all the research gets funded through this mechanism, I

can't say for sure how it's going to roll out over time. It's big right now, it's the majority right now. It may shrink some as we get clearer and clearer about high priority areas.

This is the second approach to funding high priority research. It's actually the approach we're here to talk about today, and yesterday, as a matter of fact, so this begins with PCORI engaging with stakeholders to generate research ideas, to identify the research ideas, and then to prioritize them.

Yesterday we met with a large group, I think there was maybe 120 people or so here, and they came from every stakeholder group that we know, every stakeholder group that we have -- patients and clinicians and caregivers and healthcare systems, insurers, employers, policymakers, the research community, industry, all represented here yesterday.

They proved, among other things, that they can really generate research questions. So, you do not need to worry that there will be a shortage of

research questions to prioritize when we sit down to prioritize. There will be an abundance of research questions.

So, the process, though, and the process we're here mostly to talk about today is that second part. Given that we have a lot of research questions and they span a very broad range of potential clinical conditions, research methods, and kinds of questions, how do we prioritize them?

Once we get past that process of prioritizing, the rest of it is pretty straightforward. PCORI writes very specific funding announcements. Researchers get together with patients and stakeholders and write applications that respond and those same types of peer review panels review the applications and fund the best applications.

And, again, we have a set of high priority projects funded and -- although now they're in a much narrower area driven by our prioritization process. So, those are the two ways we're here today to talk about, the more complex of the two,

in our view, this process in which we start by identifying the questions and prioritizing them.

I mentioned the review criteria, and I'll just briefly go over these. I think Rachael's going to go into more detail on them.

The first is that the questions must be patient-centered, they must be important to patients, they must consider the outcomes that patients value. Impact on the population and on individuals' health simply means, and this is very familiar to you all, it means this is a common condition or this is a costly condition or this condition leads to a lot of suffering or it's because questions are unanswered it leads to more suffering than it ought to. This condition needs attention from an individual patient point of view, from the nation's perspective.

The third one we call differences in benefits and harms and reduction in uncertainty. So, I'll try to explain that. Rachael will do a better job than I do. Everybody knows what it means, it's a little tough to say. Differences in

benefits and harms means that you have some reason to think that this research is going to upset the current understanding of the relationship between two approaches to care. It may be the case that right now we're walking around thinking that these two approaches are similar and so there's a lot of uncertainty. Some clinicians and patients are going one way and some the other, but we have a suggestion or suspicion that that may not be the case. One may really genuinely be better than the other, vice versa, it may be that right now care is being delivered with the conviction that one is better than the other but something in this application or this research idea says that may not be the case, these really may be similar.

So, research that might change our understanding of the relative benefits and harms of two approaches and thereby change practice. And secondly, and in the context, reduce uncertainty about that relationship.

The next is implementation and practice. If we do a study and find either big differences or

no difference, what's the likelihood that that information is going to be taken up into practice? Are there barriers that just won't be able to be overcome? So, that's another criterion. We want research that can change practice. In the perception of those prioritizing, this is just not going to change regardless of the research, that would move it down a notch in prioritization.

And the last one is duration of information. Is this information likely to stand the test of time? Is it going to be important? By the time the study can be done, is it still going to be a relevant question? Is there a new technology coming along that's going to make the whole research area moot?

So, those are the five key criteria that we think need to be applied in the course of identifying the research questions that we want to fund. This is going to be done with a multi stakeholder process, that's what our mission says. We start by generating those questions coming from all corners of the healthcare enterprise. We bring

together patients and all other stakeholders in multi stakeholder panels to do this prioritization, and the prioritized list of questions goes to our Board of Governors and it's the Board of Governors that makes final decisions about whether to fund -- to prioritize high enough for particular allocation of funding one or more of these research questions.

I will just remind you though that -- and I said this yesterday -- because not everything, even not everything that's prioritized highly, is going to likely get targeted funding, we still have, and I'll remind you of that, the investigator-initiated path, so good ideas still can get to PCORI, can still get funded through that path if they don't come through this top down prioritization process.

Okay, so characteristics of the research prioritization process that we should just keep in mind today are that this has to be a process done in the open, that's one of the reasons we're webcasting today. We webcast most of the meetings that we hold. And it has to be fair, and that's

going to be challenging, that's part of the methodology. How do we bring people together, all of whom have irons in the fire, all of whom have either a condition that they're most familiar with and most concerned about or a specialty in healthcare that they're involved with? How do we go from that to embracing a set of criteria and considering all questions fairly?

It's got to be scientifically rigorous and I recognize that science in this area of prioritization is still mixed to a substantial degree with art and it's probably going to be that way for a while, but to the extent that we can learn and be consistent and be reliable, that's a very good thing.

It has to engage multiple stakeholders. It does not -- it's not going to work, we're going to fail, if we don't keep all stakeholder communities at the table. And it needs to help PCORI fulfill its mission and our mission is, in fact, to change healthcare, to be able to demonstrate that the research we've produced has

been incorporated into practice and has changed practice. That's actually in the legislation.

How's it going to be put into place? In early 2013, and the Board has -- at our Board meetings we've gone through this in detail, we are creating advisory panels linked to each of the priorities. By the first quarter of 2013, we will have begun composing at least the first four of these prioritization panels, so the panels linked to the first four priority areas, and those will be, as I've said, multi stakeholder panels, they'll be peopled with individuals who have particular interest in, for example, healthcare systems, or disparities, or communication dissemination, and those are the panels at which the prioritization processes we discuss today will be put into place and implemented.

Just to say here that PCORI will continue to be about gathering the diverse perspectives of the patient and stakeholder communities. We've been doing that since very early on. Each time we have one of these meetings there is a sense in the

room that this is different, there's an energy in the room. We need to sustain that. Our sense now, I think, is that we need to actually build on that energy and begin creating a very concrete, recognizable process that people begin to know and I would say, more than anything, that's what we're here today to do, to consider the experience of the pilot process and to begin to create version one of PCORI's research prioritization effort.

So, Paul, that's it, and unless you think there should be any time for questions, I'll turn it back to you.

DR. WALLACE: We might have time for one question if you want --

DR. SELBY: I see it's the top of the hour so probably just move on? Burning question? Comment? Thank you very much.

DR. WALLACE: Great. Thank you. And, as you'll see by looking at the agenda, we'll have plenty of chance to also speak with Joe later as we hear the synthesis for the day toward the end of the session.

But I wanted to build on, again, the logic model for the day, which is to create context. I think Joe has spoken eloquently about what the need is and what has happened so far. The what always has to be followed by a how, and that usually is a staff function, so we're going to hear next about how we're addressing the how, how's this all going to happen? What's the process going to be? How are we going to move forward? And the person who has the opportunity and accountability of that is our next speaker.

So, Rachael Fleurence is a senior scientist at PCORI. She also is leading the research prioritization work and she's going to take a few minutes here to share with us the progress that's being made and also where she sees some of the challenges, and I think we'll have a few minutes for dialogue after Rachael shares her comments.

So, Rachael, let me turn it over to you.

DR. FLEURENCE: Good morning everyone. So, I've had the pleasure of working with many of

you over the last few months on various aspects of this process, so it's great to see everyone in the room today and thank you for making the trip to be here to work with us today to finalize this process.

So, as Joe mentioned, PCORI's mission is to produce and promote high-integrity, evidence-based information that comes from research that's guided by patients, caregivers, and the broader healthcare community. So, what I'm going to talk to you about today is PCORI's proposed process for doing this prioritization, that's going to help us both identify critical questions but also select and prioritize them.

So, the outline of my presentation is going to -- I'm going to start by giving you the big picture of our process, so what happens to the questions that come to PCORI and how we're thinking about this prioritization process.

I'm going to orient you to where we currently are in this process and then I'm going to share with you the results of the pilot study that

took place over the last two months and I'm going to share some feedback that we received from the participants on this process.

And then, finally, I' going to give you some of our next steps, so what's going to come out of today's meeting as we move forward with this.

So, in terms of the big picture of our process, PCORI is embarking on sort of a topic generation exercise whereby we're reaching out to the wider patient and stakeholder community to hear from them what questions are important to them. So, what are the questions that matter to them that they would like to see PCORI funding research about?

We have several vehicles in order to do this and you don't need to read all of the vehicles on this slide, but one way is that we've opened up a webpage that's written for the level of patients to be able to submit questions that are important to them. We're also going to be working with social media to send out challenges in order to work with the wider community to gather questions.

We have workshops such as the one that took place yesterday where we spoke to various stakeholders and various constituencies and asked them about the questions that matter to them.

We're also building on prior experience, though, we're building on the experience of agencies such as NIH, AHRQ, the Institute of Medicine's 100 questions, so that we're not reinventing the wheel, but we're starting from what we already know out there are burning questions.

The second stage in our process is what we're calling a gap confirmation process. We'll be getting many questions from the field, but some of these questions are not going to be research questions that are actually unanswered. So, we may find that some of these research questions actually already do have evidence to answer them and then we're looking at a dissemination issue, not an issue of generating new evidence.

Sometimes there will be a number of studies in the field that already exist and we may need to do an evidence synthesis or a systematic

review and not generate primary evidence, so in that second step, we'll be looking at confirming the research gap.

In our third step, and that's what we're really here today to talk about, is how do we prioritize these research questions. So, PCORI has limited funds and will not be able to fund everything. How are we going to find the right fair and balanced way, but also informed by science, to prioritize these questions?

And then in our final step, as Joe mentioned, the selected research questions will go to our Board of Governors for their final selection of key questions, which will be the subject of funding announcements.

And then once these funding announcements are out there, investigators matching with patients and stakeholders, will go through the regular process where they submit applications to answer these research questions.

So, I wanted to take just a few minutes here in the presentation to talk to you about some

of the principles that are guiding us and these principles are ones that we elicited from patients in the workshop that took place in October. So, we gathered close to 150 patients and stakeholders in Washington and we talked to them about what kinds of principles should be guiding us as we seek to identify and prioritize research questions.

And the three themes that came out were those of transparency, efficiency, and collaboration, and we were asked to really ensure that we were transparent in how we were doing things, how we were going to go through this process, so that's, in part, why we're here today, but our process will be up on the web, we'll find other ways to disseminate it, but so that everyone can understand how we're addressing this issue.

They also, in terms of transparency, they also talked to us about sharing the questions that we received back with the community. So, PCORI will not be able to fund everything, but let us share what we're hearing from the field back to the community so that other agencies, other

investigators, will be able to look at these questions.

Efficiency refers to what I mentioned earlier, so not reinventing the wheel, so using what we -- leveraging what we already know, what have the other agencies that have been working on this before us learned about this process, so using the knowledge of NIH, of AHRQ, of the IOM, to identify the right questions.

And then collaboration, we heard a lot about -- from patients saying, match us up with clinicians, with researchers, so that we can give you better questions. So, finding a way for PCORI to have an enabling role in that process.

So, to orient you to where we're at exactly in this process, I'm showing here a timeline. In August and September we put together a first draft of a process. It was reviewed by a number of experts, by a number of our colleagues, and it was then piloted in October and November by 35 multi stakeholder group, and a lot of you in the room today participated in that process.

Today is our workshop so that we can continue to hear your feedback, feedback from experts, feedback from the pilot participants, feedback from other people in order for us to fine tune this process so that it's ready in January and February to be rolled out to our future advisory panels.

Part of their task is going to be to sit down and start prioritizing some of -- these questions that PCORI is receiving.

So, I'm going to talk to you now about this pilot process. As I mentioned, we piloted it between October -- August and November of this year. We had an open application form on our website and 160 people applied to participate.

We took a lot of effort to make sure we had a diverse composition and a diverse group, and we were able to select 35 people who worked with us for two months on prioritizing this process.

The original task was, we gave people eight criteria to think about when they prioritized ten topics, and I'll talk to you a little bit more

about that later. Today I'm going to show you the results of that pilot process and share with you the feedback that we've already received on how this process worked for people.

So, I wanted to spend just a couple of slides on the composition of our pilot group. So, when we asked people for their primary affiliation, over 50 percent of them affiliated as researchers, although we did have, as you'll see here, close to 20 percent of caregiver and family members.

However, when we asked folks for their multiple affiliations, you'll see that there's quite a different picture here. So, close to 50 percent identified as patients and consumers. Close to 71 percent identified as researchers. And almost 42 percent identified as clinicians.

So, I think the lesson here is that people wear multiple hats and people interested in working with PCORI wear multiple hats and we're really tapping into peoples' various experiences and knowledge when we're doing this process.

The process that we had people work on was

not pulled out of thin air. There's been work in the science of research prioritization that's taken place over the last 10, 15 years. So, we used the work that's in the scientific literature. We also, for those of you who are familiar with our Methodology Committee report, there's a full chapter on research prioritization. We built upon that as well when we were developing this process.

And, again, I always want to mention the experience that we've gained from other agencies going through these processes -- AHRQ, NIH, also the Federal Coordinating Council for Comparative Effectiveness Research that had to go through some prioritization processes and mentioning as well the cutting edge work of the James Lind Alliance that works with clinicians and patients to elicit really good research questions for funding agencies.

So, folks were given eight criteria in order to think about the topics for prioritization. Joe mentioned them a little bit. I'm going to talk more about them in a few slides.

The criteria were based, as I said, on

existing work and particularly on a field called value of information, so while we don't necessarily need to call this a value of information exercise, many of the concepts that we're using come from that body of work.

We asked people to apply this process to ten research questions. We picked the research questions randomly but we picked them from a set of 500 questions that PCORI had been looking at over the last few months, and these are all vetted research questions, and by that I mean they are questions that did not have an answer. So, we knew that they were all good research questions in that all of them would require, potentially, new evidence to answer them.

You'll see from this slide, they ranged -- they were very diverse across conditions and diseases. They ranged from interventions to prevent obesity, to back pain in the elderly, to treatments for coronary artery disease. So, there was quite a wide set of questions that people were asked to work on.

We provided two software tools to our pilot groups in order to actually do the prioritization exercise. One was using a Survey Gizmo, and I'm just going to show you here a screenshot, you certainly don't need to try and read the text here, but they were basically given a number of points to allocate to the different questions after they'd worked through the supporting information and the guidebook process.

The second software that they were provided with was a decision analysis software called Expert Choice. So, in this software -- and there's a screenshot here on the screen -- is -- they're able to have drop down menus for each of the criteria for each of the topics. So, folks were able to use this software. And really what we were doing, and as we've mentioned, we're testing this process, so we wanted to use different software tools to see what came out of that exercise.

So, I'm going to share some results with you now. I mentioned this yesterday when I

presented this to our stakeholder group. We're really much more interested in the process of how prioritization works than in the actual results. So, while these results are interesting, they're not necessarily critical today in terms of the actual rankings that came out.

So, our group one, which was half of our pilot members, were given the two softwares to use. You'll see that the top ranking and the last ranking came out the same, so using -- the same group using different software decided that coronary artery disease ranked highest and interventions to reduce indoor air pollution ranked lowest. However, in between there, there was some variation in the ranking results even though it was the same group of people doing the ranking.

Our second group was only given the decision analysis software to work with and they came up with a different ranking, again, from group one. Their lowest priority was interventions to reduce indoor air pollution, but their top ranking was slightly different. They prioritized treatment

of ductal carcinoma in situ.

So, again, I think some of the lessons here is that different softwares produce different results, some variability in the results, but different groups of people also present different results. So, these are things for us to mull over as we proceed with this process.

We asked a lot of our pilot participants. We not only asked them to go through the exercise, but after the exercise we asked them to fill out surveys. We also had eight one-hour interviews with a number of participants in order to really understand how the process had worked for them and get important feedback.

So, we've tried to summarize it for today briefly, although we've not had a lot of time to digest it. But essentially four themes emerged. One was, participants asked us to clarify how the patient's voice was being weaved into the process and the criteria. So, I'll talk a little bit more about that when I go through the patient-centeredness criteria, but that was one thing

people asked us about.

A second theme was, we were asked to clarify the criteria, and what I'll show you today is that we reworked the criteria from going from eight down to five to make the process -- to keep the important concepts but just streamline it for people who are working with the actual exercise.

The third process was they asked us to improve the supporting information. I'll talk a little bit more about that, but it is quite challenging to provide a diverse group of people with the right level of information as they work through topics.

And then finally, we received some feedback on the different software tools that were used. I'm not going to go into that today, but we got some interesting insights and feedback into how to improve the tools themselves.

So, I'm going to talk to you now about the five criteria that we're sort of resting upon so far. As I said, we started with eight, we've streamlined the process down while hopefully

keeping the essence of what we're trying to get at as we ask people to do these prioritization processes. And we did get a lot of questions from people about patient-centeredness and about what was actually meant by patient-centeredness when they were -- when we're referring to a research question.

And there's really -- there are several ways to think about this and I think one is, is this a question that patients and clinicians are really asking for? Is research that would study this question really going to help improve patient health outcomes and patients and clinicians face day-to-day healthcare decisions. So, that's sort of one way to think about what a patient-centered question might look like.

The second criterion is impact on population and individual health, so looking at the burden of disease of the condition in terms of prevalence, mortality, morbidity, but also in terms of the impact on the individual with the condition, so what sort of impact on their quality of life

might a certain condition or disease have.

Also, remembering so that PCORI is charged with looking at rare diseases as well, so not forgetting that these are also important considerations as we do prioritization.

This third criterion is probably the most challenging one to capture and to explain and it's one that our participants, our pilot participants, struggled with, as did we, I think. Really what the differences and benefits and harms and the reduction on certainty criterion captures is, what's the current evidence base really telling us about the treatment choice? So, what do we currently know and hopefully what do we currently know using systematic reviews of the evidence that are out there? What do we know about the quality of the evidence base?

And to what extent would health outcomes that are important to patients be improved if we conducted research on these treatment options, on these alternatives?

In terms of the uncertainty surrounding a

research question, there are several ways to think about that and there are several ways that this may be reflected. So, one, are we hearing about -- there is a lot of uncertainty from patients and clinicians in that they're really asking to answers for these questions, but we may also look at whether there are high variations in clinical practice that may indicate, again, that there's a high uncertainty with this question.

So, there's different ways to approach characterizing this question, although we did find, once we were trying to apply this criteria to actual research topics, it really was quite challenging to describe that.

The fourth criterion is implementation and practice, and that gets to not doing research for research's sake. It's really about how likely is this research going to improve clinical practice and going to improve patient health outcomes, and it's a really critical criterion for PCORI, but it should also be critical for any agency making funding decisions for research.

Our fourth [sic] criterion is duration of information. That, again, Joe described this well. It's really about making sure that we don't fund research whose results are not going to be valid or be obsolete by the time the study results are reported. Again, it's not necessarily an easy criterion to describe a priori. We can think -- in part because different study designs will take different lengths of time as well, so then it gets a little confusing, but it is really an important criterion to think about as we prioritize research questions.

We provided ten, what we're calling, topic briefs to our pilot participants when they did the exercise and we -- it was a really humbling exercise to try and put together these topic briefs to present to people and certainly a lot of our pilot members struggled with the level of consistency between the different topic briefs and really how we operationalized the criteria to actual examples.

And I think this is no easy task. I think

that's definitely where a lot of our work and our efforts will have to focus on is how to provide good information to a diverse group that's going to be working on thinking about what research questions really matter to PCORI.

So, I think I wanted to just provide you an illustration of where we're thinking and how we're thinking about the information when it actually applies to a research question.

So, we looked at different radiation therapies for prostate cancer, and in terms of patient-centeredness, this is a patient-centered question because there really is no good evidence right now to help patients and clinicians make decisions between the different radiation therapies that are available for the treatment of early prostate cancer.

The question has been identified in AHRQ's Future Research Needs reports, it's been identified by patients and clinicians. We've actually received some of these questions on the PCORI website about asking about what are the best

treatment options for early prostate cancer.

In terms of impact, this is a more simple criterion to illustrate. We know that prostate cancer is the most common malignancy in men, over 32,000 deaths a year can be attributed to this condition. It gets challenging when we have to compare across diseases, so we will have to work on making sure that we consistently report impact across diseases when we ask people to prioritize a number of different topics.

The differences in benefits and harms and the reduction uncertainty, for this particular research question on the different radiation therapies for early prostate cancer is -- well, we can think about it, about what do we currently know about the harms and benefits associated with these treatments, and current systematic reviews have really shown that we don't know what the relative treatment effectiveness is between the different modalities.

There's a lot of adverse effects associated with the different treatments and these

adverse effects are important to patients, so it does become important to have evidence on the different benefits and harms that may be associated with these different radiation therapies.

The probability of implementation in practice, we can think about that a priori before we have any evidence to actually make changes into practice, but we can think about this in terms of the barriers as well that may face research results, even good research results. Some of these barriers may be due to the financial incentives and the way the hospitals and providers are set up right now with treatments, so these are items that we need to sort of think about as we look at these research questions. So, are there going to be any barriers that really prevent good research results from going into practice?

And then finally, when we think about duration of information, again, this is not an easy question to answer. It may depend on the study design that we use to try and answer the question as well, but for radiation therapy we know that the

technology is improving quite quickly, so we'd really want to be thinking about whether a study can provide important results before the technology had changed again.

So, I'm going to finish with just some of the next steps that await us. Today, we have all day to talk more about the feedback that you can provide to us, both on the science of prioritization, but also on the involvement of a multi stakeholder group in conducting such an exercise.

We'll have some time after this to revise what we -- revise our process in the form of the guidebook that the participants received, so we'll have some weeks to work upon that and to finalize our first process.

And the -- I'll finish with our -- the big picture of our process, which will be taking place early next year, whereby, after identifying the questions, we'll be sending these to our future advisory panels to actually go through these prioritization exercises. So, this is what PCORI's

work is going to be in the next -- early winter of 2013.

And finally, I'm just going to thank everyone in this room who's participated in one way or another in this process. If you haven't, let me know how you've managed to escape doing work for PCORI.

We have the 35 pilot members in the room. We had a technical working group that was made up of Board members, Methodology Committee members, we had a patient stakeholder on the group, Linda Morgan, who's in the room with us today. We had a representative from the American -- the APA, Neil Kirschner, who was unfortunately not able to join us today.

We had many staff members, Board members, Methodology Committee members help us along the way, and then a final thanks to NORC, at the University of Chicago, who helped us take notes and conduct interviews with people along the way. So, thank you.

DR. WALLACE: I think we have time for a

couple minutes for questions, and if no one out there has one, I'm probably going to have one. So, here's your chance. So, please, we'll get you a microphone and please identify yourself. Do we have the mic? Here it comes.

DR. LAUPACIS: Andreas Laupacis, University of Toronto. Thanks very much. I was just wondering, in terms of the briefs that you sent out, because I wasn't part of this process, it strikes me as a really almost overwhelming job to put those together, and given that you're going to have to do many of these in the future, can you give us a sense of how long it took you to put those together?

DR. FLEURENCE: So, the short answer, it took us about a month, but we were not -- well, it took us about a month. We were fortunate in that most of the questions came from already conducted, systematic reviews, so we did have a good sense of the evidence base and we were able to -- I think that's why we were able to do it in quite a speedy fashion.

However, I think, I mean, it's fair to say that it was a humbling experience and we weren't happy with -- I think we could definitely have improved upon the topic briefs that were sent to our participants, but that's part of our learning process.

We'll have to think about how many topics we can reasonably do. I mean, I think that's sort of an operational question, how -- what's the reasonable amount that we can create for our advisory panels and then what's a reasonable amount of work to ask the advisory panels to work upon. I think our pilot participants would probably say that ten was quite enough in terms of the work that that required.

MR. WALLACE: Back there and then maybe up here.

MR. MILLER: Is this on? Yeah. This is Mike Miller at Feinberg School of Medicine, Northwestern University, and Lurie Children's Hospital. I have a question about the duration criteria.

It seems to me there's an intersection, and the prostrate radiation research is a good example of this, there are -- the duration maybe both short and intermediate term, but also long-term, that goes way past any feasible studies so that a lot of healthcare issues, such as prostate cancer or cardiovascular health, will take decades to determine differences between different treatments.

I don't know how one addresses that and I don't have an answer, but it must be some type of intersection between epidemiologic studies and comparable effectiveness research, and I'd welcome your thoughts as to how you're going to grapple with answers that may take decades to find out.

DR. FLEURENCE: So, I think we don't have exact answers yet as to how we're going to operationalize all these criteria, but what's really important for us today is to start on that journey of saying, it's actually really important to think about duration of information when you embark upon a research study, so at least sort of

getting the conversation started. Whether we'll be able to answer and provide the right level of evidence for all these criteria, I don't know, and certainly we're still learning how to do that. But I think the first step is really to start thinking about prioritization differently, and that's where we're at right now. Any feedback that we get on improving how we operationalize criteria is definitely welcome.

DR. WALLACE: So, maybe we should move ahead. What you can't see is we have a little red, green, and yellow light up here and the red light now is now doing this. So, I think that means we need to move on.

Thank you very much, Rachael.

So, I think, so far we've heard from Joe about what we need to do. We've heard from Rachael that there are some significant questions around how, and I think the metaphor of seeing this as journey is absolutely appropriate. It's a journey that we're in the middle of.

There is another dimension of this, which

is why it's important, and I think our next speaker will be quite helpful to us in thinking about that added piece.

So, Gail Wilensky is an economist and senior fellow at Project Hope. I think she's well known to most people in this room, but just to highlight, I think, why she can be very helpful to us is that she's provided leadership in American healthcare now in many different ways, organizational leadership as the administrator at HCFA, leadership and governance and advice in roles as diverse as thinking of military health and also thinking of things that are close to many of our hearts in health services research with the board at Academy Health, and then, most importantly, thought leadership around health reform, around military health, and particularly, in recent years, around comparative effectiveness research.

So, let me turn things over to Dr. Wilensky. Thanks.

DR. WILENSKY: Thank you, Paul. It's a pleasure to be with you this morning. When I

discussed what I might say with Joe and Michelle Orza a couple of days ago, and we decided that since you're probably going to have PowerPoint most of the day it would be okay for me not to use PowerPoint and just talk to you.

As some of you know, this is an issue that I have felt very strongly is part of the solution for the United States for learning how to treat better and spend smarter.

The "treat better," I'm going to explain how I see this happening. The "treat better" may be more obvious of the two. I'm going to explain a little bit about how I see using this information to spend smarter, even within the context of the constraints that are placed on PCORI as part of the law, which, as again some of you know, I fervently support as the best way to make the long-term survival of PCORI increase over its other opportunities. I don't want to go so far as to say assure it's long-term survival, because I think that PCORI is, and for some substantial amount of time, will remain quite fragile, but I think how it

was set up was actually very important for its, at least, initial survival.

When people have asked me to discuss how I think this area of comparative effectiveness research is doing, my comment usually is, so far, so good, and that's honestly how I look at it. It is an area that, I think, along with improved financial incentives provides as much hope for the United States learning how to do things smarter and encouraging both clinicians and patients, with the right financial incentives, to adopt some of what comes out of comparative effectiveness research and favorably impacting spending as a strategy -- as any strategy that I know.

I don't want to go so far as to say I think it will resolve some of the most fundamental problems that we face in this country, but I see it as more likely being successful than almost any other strategy that I can come up with.

So, as I look at what's happened now, it's a huge win that comparative effectiveness research and PCORI, in particular, was part of healthcare

reform. I think, in general, all the right features are included, that is, it's a focus on alternative ways to treat medical conditions. It includes medical procedures, whereas most countries focus almost exclusively on drugs and devices, in part because they control the other stuff, which is where most of the spending occurs, with direct controls.

For us, as a country that has not engaged in direct controls in hospitals, in the amount of high tech facilities that are available, looking at alternative ways to treat medical conditions broadly defined becomes really critical, much more so than for other countries, although the UK now is moving somewhat into that broader direction.

And I have thought for a long time, as some of you have heard me speak, that the most critical role for an entity like PCORI is to be information-generating and disseminating and not decision-making, and that the worst thing that could happen to PCORI would be to have it make decisions about coverage or reimbursement.

Now, in part it may reflect the experience I had in the late 1980s, early 1990s when attention was first being given to the notion of developing clinical protocols and the question arose then as to where should that happen. And what was almost uniformly agreed to was anywhere but the payer. So, the one place that the development of clinical protocols could not be was in what was then called HCFA, what is now called CMS because as a major payer, that work would be fundamentally questioned as to whether or not it had ulterior motives.

And I think that much is true in a similar vein for PCORI. Its role, as I look at it, is to provide as good information on comparative clinical effectiveness, of strategies that will involve alternative ways to treat important medical conditions as we can find, and anything and everything that can be done to protect the purity of that information from being regarded as tainted by payers, is really critical. So, you will not be surprised when I say that some of the constraints that have been placed on this through legislation I

regard actually as great favors for at least your initial survival.

Having said that, I would be misleading you if I didn't say, the concept remains controversial. There are a variety of limitations on what PCORI can do, which will make some challenges, and as has already been mentioned, and I'm sure will come up later, how to try to get the information that comes out of PCORI to be useful in decision making by the people who actually make the decisions, either the payers or clinicians or patients is going to be a big challenge.

And it's fragile as an idea, in part because it is not something that this country has actively embraced as an important function for government to be involved with, and it's fragile because the funding is just so limited and pitiful. I can say that since I'm not involved in those decisions, but it is very frustrating when you think about how much we spend on healthcare in the United States and how very little we have traditionally been willing to spend outside the

biomedical research area in terms of how to spend smarter.

It's been a problem for ARHQ for decades. I was there in the mid-1970s for eight years, and every single year we used to have retreats, it was then called the National Center for Health Services Research, for those of you around who are old enough to remember, and every single year when we would have these retreats, we would try to wrestle with the question of how to make it clear how important health services research could ultimately be in order to try to get a smarter healthcare system in place, one that was more efficient and effective, and bemoaning the fact that it was very hard to get sponsors comparable to the sponsors that NIH had been able to maintain.

That remains a real challenge for a group like PCORI, although it is potentially more directly involved -- that's the good news and the bad news.

Now, I know that you're going to spend most of your time today on this issue of how to

establish prioritizations. I just want to say that ultimately, for me, the question you need to be able to respond to affirmatively is that when you look at the choices they meet the general criteria that there are significant variations in terms of how that medical treatment or medical condition is treated across the United States, and those variations have consequences. They can have consequences in terms of patients' outcomes and well-beings, and presumably they will have consequences also in terms of the economic implications of these alternatives.

To my mind, after you go through all of your prioritization, and you will have to balance the need to get buy in with the need to have something to show for yourself, I will leave it for you to decide how to weigh those two pressures, but at the end of the day, if what you're looking at can't pass those general tests that how that medical condition is treated very significantly across where you look, not necessarily geographic variations, although usually that's a part of it,

and also is important, as a result, to understand these variations, as I've said, either because of the impact on patient outcomes and/or the impact on economics, then you need to be thinking hard, even if it is a popular area, why, given your limited resources, it's an area appropriate for you to focus on.

Now, one of the things that's already been mentioned is that it should be possible to learn something from the stimulus bill in terms of how they made some of their decisions, focusing on what goes on in the real world, the need for coordinating and then their need for having strategic frameworks. I think that's useful guidance to see how they've done.

I'm getting a little frustrated that a statement I was looking at, some slides I had put together quite soon after the Affordable Care Act was passed, and commenting then that it was too early to know our results. Well, here we are more than two years later and as best I can tell, it seems still to be too early to know the results of

the comparative effectiveness research that was funded by the stimulus act.

Again, this is an area that is going to be important to remember that at some point, probably a lot sooner than you would like, the PCORI judgment will be made about whether or not useful activities are being undertaken. And so, again, I appreciate the interest in trying to make sure you have buy-in by the various constituent groups that are affected.

I hope there will be equal concern given to the fact that at some point the Congress is going to judge as to whether or not what you are doing looks like it's not only not offensive, but is actually likely to produce good results, and making that tradeoff will be very important.

I thought early on the fact that the studies that the stimulus bill funded included a mix of randomized clinical trials, but also those studies which did not lend themselves to being looked at via randomized clinical trials, is exceedingly important. This issue about what

provides credible evidence is going to come up for you, obviously, as it will for those studies.

It is an issue where there still seems to be enormous controversy, particularly among some of the most staid biostatisticians that, at least, I run into. I've had some very, let's say, spirited discussions about why randomized clinical trials can do very good things about controlling for selection bias, but frequently they do not do a very good job about providing information that actually captures the variations that patients present when they present themselves for clinical treatment. And so, the relevance bias versus the selection bias is an issue that needs to be given more thought and care than sometimes goes on at purely methodological discussions, at least from my point of view.

It's important to recognize that some of the studies, no matter how much buy-in and how much prioritization you get into, can and probably will be controversial, and the more they go against conventional wisdom, the more likely that is to be

true. You need to be sure that you are able to say, "We have had input from the affected parties." It is certainly likely to be true for you in a way that hasn't always been true because of the very extensive process that you are using with the patient community, but that doesn't necessarily mean all of the affected parties will feel that they have been consulted as well. And how you disseminate your findings and the explanations will be very important. I found that the flat controversy that came up after the Preventative Services Task Force disseminated their mammography guidelines was a very serious wake-up call for all of us who are interested in comparative effectiveness research. That what to me was a very thoughtful, well written report for probably the ten of us that actually bothered to read the report itself, was very different from the way it was characterized by the media, but helped along by what I regard is an incredibly tone deaf group in terms of when and how they release their findings, not making clear enough to people who might want to

misuse the information, why what looks like similar evidence was being associated with what looked like very different recommendations, although actually they weren't. And it was just a real wakeup call as to when some individuals' economic interests may be negatively affected, or past physicians and stakes in areas are being challenged, you need to be very thoughtful and careful about when and how precisely you disseminate information. It's hard to imagine you won't have many opportunities to learn this on your own. Hopefully, you can learn from the stumbling of others.

Ultimately, the real challenge, of course, is how can effective use of comparative information, comparative clinical effectiveness research, be used to both improve health outcomes and -- I'm an economist after all -- to help us learn how to spend smarter.

Now, actually, it has always been a little easier for me in dealing with this question as an economist, at least at a conceptual level, because I have always thought about comparative

effectiveness research as being more useful in terms of reimbursement rather than in terms of coverage.

For me, whether or not something should have an FDA approval ought to be subject to no more than the current FDA requirements in terms of safety and efficacy. Whether it is covered under Medicare or other groups, it's certainly legitimate to say, were the trials covering the population relevant for us, which is clearly not always the case for drugs or devices that may have had the clinical trials focused on an under-65 population or another population not well represented, for example, by the Medicare population.

But beyond that, the question, to me, is not whether or not it should be eligible for coverage, but how should you reimburse for this new drug or device. And that's where comparative effectiveness research can really be helpful, because there you can then ask the question, does it appear to do more? And if so, do more for whom? And with what kind of clinical certainty are we

discussing this? And it is at that point that the potential usefulness for comparative effectiveness research, particularly for the comparative clinical effectiveness, really becomes much clearer.

Now, we need to recognize that if there is any hope in order to get these ideas being a part of the thinking of clinicians and patients, it's going to be very important to get physicians as a part of the process and to feel that they've had some buy-in, and particularly if conventional wisdom is being challenged. And similarly for patients and advocacy groups to be comfortable that the questions you are asking and the data that you looked at really does include patients like them.

Now, you've heard, I've heard, ad nauseam, these concerns about just looking at average patients, and the answer is, of course, that is not the purpose of doing that, but rather to distinguish when there is variation as to which groups, however we are able now to define these different groups, appear to be helped differentially and at what kind of a likelihood are

we talking about.

Typically now we are describing individuals either in terms of social-economic characteristics or in terms of co-morbidities. At some point in the future, it may become increasingly possible, as it occasionally is now, to look at gene basis for distinctions, to look at metabolic classes to help distinguish differential responses, but we can only go to where we are as we make progress on those fronts.

We should be able to differentially describe people in the characteristics that matter in terms of that particular intervention.

As I had mentioned earlier, I understand and actually am extremely supportive of the fact, that PCORI can't mandate coverage and can't mandate reimbursement and that CMS, at least, is unable to use cost either in terms of the coverage decision or even use comparative effectiveness research directly in any way in terms of reimbursement. And that, of course, makes it more challenging for the public sector.

I do think, in the short-term, at least, but maybe in the long-term as well, that the separation is very healthy. To me, the most important change that needs to occur is to get people thinking about comparative clinical effectiveness and how new interventions may differentially affect different groups of people and trying to understand what the relevant groups are that are responding differentially.

There has been a lot of discussion about whether or not you can have useful decision-making occur without cost effectiveness analysis. This is something Joe and I were recently having a discussion, and my view on that is that these decisions, with regard to cost effectiveness, can be done later, easily by payers. It's not nearly so complicated as doing good, credible, comparative clinical effectiveness research. That's the part that takes a long time and that is very expensive, and without which, the cost effectiveness information is really useless.

So, I don't regard this as a particular

problem. I think private sector payers can do this, I think public sector payers can do cost effectiveness analysis, and frequently, it will only be relevant in certain kinds of outcomes for comparative clinical effectiveness if there's basically no difference, then the cost, obviously, is something you ought to concern yourself about.

There is a substantial difference for at least some subgroups of the population. It's unlikely, at least in this country, that differential cost effectiveness analysis will impact decision-making in any case.

Fortunately, the same kinds of constraints that exist in the public sector don't exist in the private sector. I'm a real supporter of value-based insurance and value-based reimbursement, and this, to me, is the perfect pairing of comparative effectiveness research with value-based insurance. When you have clinical interventions that look like they are highly likely to be beneficial, you want to encourage their use, you want to have very low or no copayment, and you want to make it widely

available and encourage its use in terms of value-based reimbursement by the clinicians.

When you have other interventions, which at least for some subgroups of the population are highly unlikely to be clinically effective, for me it is unwise to say no. That is not a popular word when it comes to medical interventions in the United States. But there isn't any reason why at least private payers and maybe ultimately Medicare shouldn't be in a position of saying, but we are not going to provide the same kind of funding support that we do for those things that have a strong likelihood of having significant clinical improvements for patients in a particular subgroup.

And so, encouraging the private sector to use comparative effectiveness research, not just in its coverage, but how it actually does reimbursements, is an important first step. It might be possible in this era of supporting pilots and demonstration projects of all sorts to try to determine whether the concept of value-based insurance in general could be used in Medicare. It

would set a very important precedent for Medicare, which ultimately would require new legislation to be generalized, but you'll recognize that that is at least a first step to try to have Medicare reimbursement take account, not only of safety and efficacy, but whether or not an intervention is likely to be clinically effective.

Unfortunately, in this area, as so much of when you work in healthcare policy, you're going to need to focus on the long run. These are not changes that are likely to occur quickly, but when I consider the alternatives, which are primarily focused on trying to impose global budgets, much tighter payment controls across wide areas of the provider community and across payers, trying to get better information about what works when for whom under what circumstances, and to put it together with financial incentives that encourage the use of the most important clinically beneficial interventions and discourage, but don't prohibit, the use of those which are the equivalent of the Hail Marys, seems much likelier to have a chance of

survival in the United States than some of the direct control mechanisms. I am mindful that people in political roles are getting a little impatient about trying to get our arms around healthcare spending, so while you are doing your activities in a clear and deliberate manner, my final words of advice is, don't go too slowly.

Thank you very much. We have a few minutes left.

[Applause.]

DR. WILENSKY: It says I have three minutes, so I can have one or two short questions. Yes.

DR. MELTZER: I'm David Meltzer. I'm a member of PCORI [off microphone].

DR. WILENSKY: Right. Nice to see you, David.

DR. MELTZER: [Off microphone.] And as the only economist on the PCORI Methodology Committee, I feel genuinely grateful but also obliged to ask you the following question.

When you framed the issue around PCORI

setting coverage policy potentially as a challenge early in this debate, or something that would become PCORI, you emphasized the risks that come in setting limits.

But the legislation says that PCORI shouldn't use its analyses to set coverage policy. But the way PCORI has gone about implementing its charge has gone even beyond that, to the point of saying that it won't study the costs of a treatment unless those costs are directly to the patient. And I'm curious how you feel about that extension of the limitation. Do you think it's necessary in order to protect PCORI politically? Do you think it's scientifically appropriate?

I'll express my bias very openly, which is that I actually think it's very hard to figure out what the costs are of interventions because they have a whole series of consequences. Those consequences aren't clear, and so without them it's really hard to know whether one treatment is, you know, cheaper or more expensive than the other.

And I guess I'll go just one step forward,

sort of laying it all out there. To me, the total cost of healthcare is a patient-centered outcome because the last time I checked, health insurance, whether public or private, is ultimately paid by people.

DR. WILENSKY: Of course.

DR. MELTZER: And it's taken out of their check every month. So, to me, I feel like we may have gone a little too far on this and I really, particularly given your importance in this, feel obliged to get your opinion about this.

DR. WILENSKY: Well, the way I regard it as relevant to PCORI is in trying to decide what areas to look at, and that's why I said early, it has to be an area in which there are substantial variations in how a medical condition is treated and they have to matter, and the way they have to matter is either because there is substantial impact on patients' well-being or because there are substantial economic implications, and I certainly did not mean only to the patient in terms of these variations in treatment.

That means that there's some great uncertainty about how things or why things are done, and that puts it up for study. It's what happens after that and that's where PCORI should stay far, far away. It's an issue that needs to be dealt with; it's not a PCORI issue.

PARTICIPANT: [Off microphone] -- with the National Business Group on Health. So, Gail, thank you, you know, for putting your great mind on this, on your comments today. I wanted to actually go back to the value-based design and really even maybe building off the last question to say that where things seem to be going for the large employers on this is that plan design is such a blunt instrument and when we look at what's really happening with comparative effectiveness research, there are really very few things that are so clear that we can, say, create the incentive to use it more or create a disincentive, you know, across populations.

So, I just want to throw out there that I think what we are seeing now and we're going to see

more in the future, is the plan design incentive is for people to use decision support tools and shared decision-making, not whether the intervention is covered or not, but to use decision support, and I think, actually, that's the best case scenario considering a lot of what we see are inconclusive results or things that are so determined on your individual situation, so patient-centered.

DR. WILENSKY: Well, okay, but we actually use tiered pricing all the time in benefit plans. I doubt there's anybody in this room that doesn't have a pharmacy benefit, that has tiered copayments except there it's usually based on what the PBM got the best buy on and what I'm saying, the reason I like the value-based insurance is, it's that same differential thinking, but based on clinical information, instead of what a buyer got the best buy on.

So, it's hardly a new thought. It's now been part of the American healthcare plan design for over a decade. I never hear people talking about this or rarely as some kind of major

rationing issue that they have zero or a $4 copayment for using a generic and a huge cost for using very expensive, non-preferred braded drug. I sometimes wonder exactly how they actually know how some of those decisions are made, but I wonder why that isn't regarded as a more serious effort.

Shared clinical decision-making is fine. I like the fact that many of the big payers now are lowering co-payments and lowering the premiums for patients who are willing to engage in healthier lifestyles or who'd go to institutions and clinicians that they have deemed, by what needs to be a transparent process, efficient clinicians and institutions. And so, it's really only an extension of that thinking and if we can wrap around that way. I know that WellPoint is doing that, Aetna has long been described as doing that, United Health Group is doing that, I mean, I assume some of the large other -- Blues plans at the state level are doing similar things.

That really has gotten away from not having people try to be impacted by the economics

of some of these clinical decision-makings, and I'm all for shared clinical decision-making, I just think it's foolish given the potential variations in the prostate cancer is one that just knocks your socks off when you look at the cost of some of the interventions for which I gather there is no currently available clinical information as to the differential effectiveness. That's a very major issue not only for the patient, but for the rest of us who are forking over the money.

PARTICIPANT: [Off microphone.]

DR. WILENSKY: Okay, I didn't hear it, but you can tell me after.

DR. WALLACE: Thanks very much.

DR. WILENSKY: Thank you.

[Applause.]

DR. WALLACE: Well, there's obviously a little more work to do, but it's also time to take a break. So, we have about 15 minutes, and if you synchronize your watches that means we're going to start again at about 20 minutes after the hour, so please be prompt.

Right after the break we're going to dive a little bit deeper into the existing knowledge base around prioritization. So, thanks very much.

[Recess.]

DR. WALLACE: One of the paradoxes of moderating is that you want to moderate a meeting that's very engaging. The challenge is getting people back to the meeting from the breaks. But thank you for your attention to the time,

So, we have another hour here so that we can dive a little deeper into what do we actually know about the knowledge base of prioritization, and we have the opportunity to hear the product of a couple of papers that are going to be shared with us.

The papers were produced by David Meltzer and then also by Karl Claxton working closely with his colleague Claire McKenna. Karl's not going to be able to join us today but Claire will be representing their work.

So, first, let me just briefly introduce and turn things over to David Meltzer. As you

heard before, David is that powerful duo of being both a physician and an economist and so probably spends most of his time trying to reconcile those different perspectives, right, and he's going to share with us the work that they have done on preparing a white paper entitled *Pragmatic Approaches to A Value of Information Analysis.*

And I would also remind you that, again, bios are in the material that's been distributed so I'll let you review those there. So, David?

DR. MELTZER: Okay, great. So, I'm pleased to be here and talk about this paper that we're in the process of preparing that really tries to lay out in a little more detail some of the pragmatic approaches that one can use to apply this concept of value of information analysis, particularly in the context of PCORI.

And I want to start by saying that value of information analysis is a fairly new method and when organizations think about using methods, it's really critical that they align with their mission. And I want to point out the example of the Centers

for Disease Control. You can see here on this slide their mission, which is this incredibly broad mission, to collaborate, to improve the health of the public, and when the CDC looks at trying to realize that mission, one of the challenges it's always faced is it's never had the money it needs to really do that.

And, you know, CDC's a lot like PCORI. It has certain legislative mandates, it has certain administrative functions and actions that make decisions, and it also uses peer review sometimes to decide what to fund. And I think it's fascinating that if you look at the history of the CDC, they've been amazing leaders in the development of new methods to inform decision-making and advocate for the things that they think are important.

So, for example, Dorothy Rice's pioneering work on the economic cost or burden of illness was worked on from the National Center for Health Statistics, a part of the CDC. Jeff Koplan, one of the CDC's directors was really one of the leaders

in the use of cost effectiveness analysis in health policy in the United States.

And this is an area where cost effectiveness really has traction because what they're asking for is money for things that truly have value rather than the situation where in healthcare often we're trying to limit.

So, my point is, it's really important for organizations to think about using methods that align with their mission.

Now, PCORI has a very particular mission, it's a mission heavily defined by addressing the needs of patients, and I know everyone in this room has seen these questions many a time, but they're great questions and they really define what does this research mean to individuals.

And so, if PCORI is going to use a tool like value of information analysis, it's going to have to address questions like that.

Now, PCORI's enabling legislation actually describes criteria that PCORI needs to use to inform priorities for research, and you see on this

slide the ones that are listed in the law, and many of them we've talked about today -- impact on health of individuals and populations, gaps in knowledge, patient-centeredness, improvability, healthcare system performance, which I think means something about resources, inclusiveness, potential to influence decision-making, efficient use of research resources. These ideas are all things that we want to get at.

Now, as PCORI has worked through the process of trying to implement these, its developed research prioritization criteria. There are many -- there are actually now several versions floating around of these used for different purposes in the sort of evolution of PCORI. These are the set of criteria that were actually listed in some of the recently released RFAs. We've talked about many of them today already and I think yesterday as well, things like the impact of the condition on the health of individuals and populations, prevalence, incidents, other measures of burden, innovation and potential for improvement.

There are others: potential impact on healthcare performance, patient-centeredness, inclusiveness of different populations. So, if PCORI is going to use VOI, it has to do so in a way that respects these criteria.

Now, the Methodology Committee has had a variety of efforts to try to inform methods for research prioritization. There's been a group of us working on research prioritization methods. This was a very early version of the sort of strategy that we developed and I think you can see it reflected, to a good degree, in some of the slides that Rachael presented today beginning with topic generation so that you make sure you're considering the right questions, gap analysis to try to figure out where the holes are, and then some sort of prioritization exercise, and we thought about the use of value of information analysis either formally or at least in its principles, and then ultimately ending with judgment in peer and stakeholder review.

Now, as this research prioritization

process takes place, as was mentioned today, there are really sort of two different broad tasks, one is to prioritize specific research studies -- should this study be funded? The other one, which I think is the focus today, is to prioritize research areas.

I'm, in some sense, going to talk about both of these, and I think that they're actually related to each other in very, very important ways, if none other, through the budget constraint because we only have so much money, but I'm going to try to talk about both of these, and I think value of information analysis is easier to ply in some sense to one to the other, but is actually relevant to both.

Now, what is this concept of value of information analysis? In a sense I want to spend most of the talk telling you about what this idea is, what it means, and sort of helping you see how to learn more about it.

So, the fundamental idea is to take a systematic approach to valuing the benefits of

research. What it does is -- the value of information does is calculate the change in the expected value of an outcome, and you can measure it in all variety of different ways, given a decision with research done versus the expected outcome of that decision without research being done.

So, what's the gain you get by getting more information? And it has deep roots in statistical decision theory in the 1950s and a whole series of us have been involved in developing it over time. And it's been widely used outside the United States, in the UK in particular, by the National Institute for Health and Clinical Excellence. Claire will talk in a minute about some of, I think, the work they've done.

And it's got growing use in the U.S. and I could talk about some of the applications. But the key idea is -- do I have a pointer? I don't think I do -- so, the key idea is really in this tree here. So, the question, in essence, are we going to do A or B? Are we going to choose treatment A

or B? And if we don't have research, we just have to guess, which one seems better? We use the best information we have, and let's say it seems like A is going to be better than B.

So, in the absence of any more research, we're going to go ahead and do A. But we have the option to do research, and when we do that research we're going to study A versus B, this is the top branch, and with some probability we're going to discover A is really better than B, in which case we're going to keep doing A. And there's been no benefit to that research except that we're a little more sure.

But with some probability we're going to learn that B's actually better than A, then we're going to change our decision. And what the value of information idea says is that it's that change in decision that's valuable. And how is it valuable? It's valuable because of the difference between B and A, how much better than A, B is, and how likely it is that we're going to change our decision, the probability that B is better than A.

Now, that assumes that our research is perfect, that it always gives us the right information and once it's done, we really know what the right thing to do is.

The reality is, that's often not the case. And so the value of information is sort of a set of compromises. We make the best compromised choice not knowing information, and then with information we make the best decision ideally knowing the true state, but perhaps even that true state, you know, isn't exactly what we thought it was.

Either way we end up with the same idea, it's the probability that research changes your decision times the expected gain if it does change your decision.

Now, what do you do when you have a lot of imperfect information? It turns out that if your research is sort of less than ideal, you don't get as much value out of it, and so often we're in that situation where we can't get the true value of information, what's called the expected value of information at the top, but we're missing some sort

of other form of information, like how confident are we before we do the research? How confident are we going to be after we do the research? How big really is the burden?

And what this slide just does is say that there's a science behind deciding how confident you can be about the value of research depending on how much information you have.

And so, you can put bounds on these things. With more information you can put a tighter bound, with less information you can only put a broader bound. And the ideas embedded in this are very complicated statistical ideas from Bayesian statistics, but one of the things you'll see when everyone gets the working paper is we're developing some very simple examples to illustrate this using nothing more than basic algebra -- in fact, not even algebra, it's just addition -- I guess division -- addition and division, maybe a little multiplication. And what these ideas illustrate is this idea that these bounds may be more or less informative.

And so, we're often challenged by the information we have, but given that, we can often provide bounds.

Now, the other -- the key thing if we're going to use this in PCORI, as I said, is it has to align with the criteria, and the criteria that I described earlier are listed here, and for a lot of them, the match of these things is very obvious, the impact of the condition on the health of populations for sure, maybe also individuals -- I'll talk about that in the end -- innovation and potential for improvement, differences in benefits, reduced uncertainty, how likely something is to be implemented, durability -- absolutely, VOI is set up to do that. The potential impact on healthcare performance, I think also, again, to the extent one thinks about costs or wants to, the potential for patient-centeredness, the potential for inclusiveness; these are more complicated issues for value of information analysis, but I think they're also addressable and I'll talk about them.

Now, before I do that, I want to give you

a sense of what these calculations actually look like because there's math here, but it's actually very intuitive, in fact.

This is an equation that describes the value of research as going from the individual level, the individual level value of information, all the way up to the population level.

So, on the far right there, the IVOI means, what on average is it worth to a single person to get this information about this study? How would we expect it to help them? And there are a variety of methods, I sort of alluded to them, for calculating this for individuals, and I'll come talk a little more about in a second.

Then you ask, how many people are going to be affected, the number, that's N. How likely is this information to be implemented? Because if no one's going to use it, it doesn't matter. How durable is it likely to be? And then you add this up over a patient's lifetime and the lifetime of a society, in a sense, and you get a value of information.

So, this is sort of the population level, and I'll come back to the individual elements, but I want to focus first on this individual level value of information and how we actually calculate it.

Now, one of the big challenges in doing these calculations is that most calculations of the individual level value of information are based on decision models, sort of statistical models that describe the likely outcomes of different decisions. And those are very complicated. And so we've come up with a variety of different methods going from this sort of, what we call full modeling approach where a decision model is built, to limited and no modeling approaches. And with my collaborators on this paper and in other work, Ties Hoomans and Anirban Basu, we've developed a hierarchy for this. This is work we originally did for AHRQ and this is published -- the only reason this slide is here to tell you that there's information available on the web about this and that you can read about it.

But it gives us ways to simplify this approach and I'm going to quickly sort of describe some of these approaches.

Now, to understand the importance of simplification, you have to first understand how these things are typically done. And as I said, the way they're typically done is by building these complicated decision models. So, this is a sort of classic paper in the field that Karl Claxton, Peter Newman and others contributed with.

So, this is a Bayesian model of the value of information about treatments for Alzheimer's disease, and what they did is they began by building a decision model that simulates how patients with mild, moderate, or severe Alzheimer's disease progress through treatments ultimately to death.

And the question is, how valuable are the set of drugs acetyl cholinesterase inhibitors in providing treatment for this, and what's the value, in particular, of more research about their efficacy?

As they developed this simulation model, they then put data into it from existing clinical trials and they calculated measures of the net benefit of the treatment. They were looking also at costs in their case. And what they found is that at 24 weeks, in the short term, there was very little question about whether these drugs were worthwhile or not. We were pretty confident that they had benefits, but they had costs, and the costs are actually pretty large compared to the benefits.

But when you go out to 210 weeks, that curve that's very flat extends both on the negative side where things are harmful and on the positive side on the X-axis, where things are really beneficial. So, there's a whole lot of uncertainty about the long-term benefits.

And so then what they did is using this model they were able to prioritize different questions that they could study, and they concluded, for example, that the total value was something measured in the hundreds of millions of

dollars of all the potential questions you could answer, but almost all that value came from extending out the duration of the study. The single most important question is, do these drugs work for more than a few weeks, okay, long-term?

So, they said, this is what we should be studying, not costs, not even side effects, that's what really mattered for the most on average.

So, this is the way this is done. The problem with this approach is you need to build a really complicated decision model. It's way too much work to do most of the time unless you have a really big question.

So, we started looking for sort of other ways to do this. We call them broadly minimal modeling approaches. And the idea here is that your estimate of the uncertainty about whether this is valuable comes directly from a clinical trial or very closely from a clinical trial rather than an existing clinical trial, rather than a simulation model.

So, one example where we've applied this

is looking at the value of atypical antipsychotics versus traditional antipsychotics. And here we have an existing clinical trial, the CATIE Study, which was a large NIMH-funded study comparing the more expensive atypical antipsychotics to the traditional neuroleptics, perphenazine, in particular, which is cheaper.

What did they find in this big study? That discontinuation rates were similar with the two classes of drugs and perphenazine -- which was what they used as their outcome measure -- and perphenazine was a cost-effective -- it was cheaper, so therefore a cost-effective first line treatment.

What are the limitations? Discontinuation isn't exactly a great endpoint. There was limited precision in the estimates of effectiveness and costs. And this limited precision is particularly worrisome given the incredible prevalence of schizophrenia. It's 1 percent of the world population, it's over their whole lifetime.

So, in a lot of ways you should worry,

should this be considered definitive? But, in fact, this study's been heavily discussed in coverage decisions and some have argued we shouldn't be studying this anymore.

So, we went to look at that.

Now, as we looked at it, we had available to us a cost-effectiveness study analysis of the CATIE study, and essentially there were two main findings. One was that perphenazine was clearly cheaper, the other is that none of the other drugs looked better than perphenazine. One of them, risperidone, looked a little bit worse, but it was probably a dosing problem.

But the key thing is, compared to the atypicals, perphenazine looked just as good and was much cheaper. So, you could argue we're done.

Well, we questioned that, and we questioned it because of this large uncertainty in variability. So, we had sort of two goals in doing this, one to figure out what would be the expected value of more precisely determining these differences, and then, secondly, to figure out what

would be the optimal sample size for a future and potentially expensive trial.

And I could certainly imagine PCORI having both these sorts of questions as time moves on.

What did we do? We used what we call limited modeling approach. We took the CATIE estimates of the effects on costs and quality of life in any given period and we built a very simple model to extend them out to a lifetime and then over the population to try to go from the individual level to the population level.

These were the estimates of the uncertainty for a quality of life for the different drugs, and you can see one drug, risperidone, did a little worse, but all the others overlap, and this is on a quality of life scale between zero and one, and the peaks look pretty narrow, like these are pretty close, the range there is like from 0.7 to 0.74, 0.75, that's a very small amount on this scale.

So, you could say, these are really pretty precisely done studies. But before you decide

that, you have to think about how many people it's applied to. And in our case, because we were looking at cost-effectiveness, we also wanted to think about costs, and the one orange curve there is for perphenazine, that's on the cheaper side, so that was clearly cheaper, but the others were obviously more expensive and had really broad tails.

So, what's the value of resolving this apparently or intuitively very small uncertainty? Well, it turned out when you added to the incident cohort, and overall that's 20 cohorts that might use this information, we found it would be worth $342 billion to answer this question in terms of health gains. This is an absolutely huge public health question.

And yet, it's not obvious when you look at the figures, and this is where analysis, I think, can really help inform things.

Now, this is one example of a minimal modeling approach. We call this limited modeling. There are also other examples I'll come to in a

minute. Let me just say that we also did studies of how big and optimal studies should be, and where as the CATIE Study was about 1,500 patients per arm. We estimated that ideal studies should be in the order of 20,000 subjects per arm. How in the world do you do a 20,000 subject per arm study? The answer is you don't do a traditional clinical trial. You probably do some sort of policy intervention. You look at a bunch of states who are pretty much indifferent between which atypical antipsychotic they use and then you do some sort of policy evaluation based on that, either randomized or non-randomized.

So, let me just say, that's the limited modeling approach. We also have these no modeling approaches, and the key idea in the no modeling approaches, you don't need to model anything at all because the trial follows people out to completion, and there are two instances in which that happens, one is where at the end of the trial everyone is dead -- so, pancreatic cancer, unfortunately, is an example where you could do something like that.

This is another one, which is a happier story, which is the treatment of sinusitis where at the end of most trials, everyone, sort of almost everyone, gets better except the people who probably just had allergies to begin with. And we compared the value of more information on azithromycin versus augmentin in acute sinusitis, where azithromycin is thought to be a little more effective and augmentin is cheaper.

And there was a small RCT that showed there were differences over the first five days, but by 28 days it had all resolved, and we did calculations in value of information looking at the net benefit, or the total benefit, if you only counted resolution of symptoms, and a measure of net benefit when you also took off costs.

And we scaled it up to the population and we discovered, for example, that the value of information on effectiveness, the study would be worth $40 million. That's a whole lot less than $342 billion.

Or the value of information on cost

effectiveness would be worth much more, $250 million. Why is it worth more? It's because there was really pretty little uncertainty that azithromycin was better, but the question is, is it worth it enough?

And in this case, one of the things this shows you is if you ignore cost from the beginning, you are forced into different research prioritization decisions, and that's something, I think, we have to worry about.

So, the most important thing about this slide is to tell you, building a decision model takes months, a limited model probably takes, you know, weeks. This probably takes days. So, this is something one can practically do if one has preexisting data.

Okay. If even that is too much, there's another option for VOI, and that's to take an approach we call conceptual value of information, and the idea here is that if you look at this value of information equation, it's multiplicative, the individual value of information, the number of

people, the implementation, the durability. And, you know, within the individual value of information, if you're not going to change anyone's decision, there's no value. If there's no difference between the outcomes, there's no value, you're done. You don't have to ask anything else.

The same to some extent may be true of the others. If no one's ever going to implement anything based on your research, if a new study is going to come next year that's going to completely trump it, if no one's affected by this -- and you'll be surprised how often no one is affected by research we do, and I can comment on that if anyone wants to ask -- then you're done.

And so the point is, there's a natural weighting scheme here. These should almost be necessary conditions for something. Now, that doesn't mean that you can't override it with judgment, but the point is, you can look at these things, intuitively apply them, and, in fact, a lot of what PCORI's begun to do reflects this sort of idea. And so it's, I think, useful to frame this

in the context of the broader question of how you apply VOI.

Now, the beauty of VOI, I think, is that in the end you end up with some numbers, or at least you can end up with some numbers, and these are a variety of normalized value of information studies where the assumptions that go in for them in terms of the year, the unit of currency, the population you're studying are all comparable. And what's amazing to me is just the incredible range of these.

I think my wife would be okay with me saying she just had knee trauma and had a really unpleasant couple of weeks dealing with it, and she's getting better now, but interestingly, magnetic resonance imaging in knee trauma is hardly worth anything on this. In fact, it's 1,000 times more important to answer this question about atypical antipsychotics.

So, it didn't feel that way in my house over the past month, but this is where numbers really, really help you. And so you can get order

of magnitude differences that help you inform these things. And I'm not saying VOI should be the only thing we use, but part of it.

Now, you know, when you get this sort of set of different approaches, you have to think about how to use them together, and these are ordered in this slide from the easiest to use to the hardest to use, easiest being conceptual, then minimal modeling, then full modeling, and there's one more, which is maximum modeling, which actually basically means build a really complicated model that can incorporate multiple diseases, maybe even -- certainly multiple questions within a disease within the same model.

And the basis for something like that would be in, for example, the Carnegie Heart Disease Policy Model that Bill Weinstein and Lee Goldman and others developed in the 1980s. It can look at all different interventions.

So, you could build a model that addresses this in a priority area and then try to prioritize questions within that, and, in fact, there are a

variety of institutes in NIH that are beginning to do exactly this.

So, then you can think about how to put it all together, and with support from AHRQ we've done some work recently trying to develop algorithms to sort of put these things together. So, you begin with sort of a potential topic for research, and then you can apply conceptual VOI and if it looks like a study is just not going to be very valuable, you're done.

If it looks like the study might be valuable, then you go to the bottom branch. There you can ask, does this topic cluster with others in some domain? And if yes, I can build a maximum model and really try to prioritize in the whole area.

If not, then you could say, well, do I have comprehensive outcome measures so I could apply a minimal or limited modeling approach, existing clinical studies? And if so, and that's easy to do, then it might be worth spending a few days to try to get this number.

If you don't have that option, then you're in a world where the only way to do this is to build a really expensive decision model, and I would say you're only going to do that if you're talking about making a major, major investment in a clinical trial. But someday PCORI may be talking about these multiple, multiple million dollar investments, and this may be a time when it makes sense for PCORI to think about that.

I'll say we've applied this approach in work for AHRQ looking at some topics that they've considered for systematic reviews and it's turned out to be a useful framework in thinking about this and one that provides insights not provided by other approaches.

Now, let me come back to the PCORI criteria. I think, as you'll see, impact of conditions on individuals -- sorry, on populations, potential for improvement, implementation, uncertainty, we've got all of that. Impact on healthcare performance, we've talked a little bit about costs.

So, the things we haven't talked about, what about individuals? What about patient-centeredness? What about inclusiveness? So, let me turn to that in the last few minutes.

So, I think one of the critical ideas in this is that it is possible to reflect individualization within value of information analysis, and the key idea here is that you need to incorporate individual level attributes into these models. These could be traditional health-related covariates, they could be peoples' personal preferences, it could also even be the choices they make if those choices somehow do or don't align with what's in their true interest.

How do you think about that? So, Anirban Basu, who's here, and I, wrote a paper a number of years ago looking at the value of individualization, and the concept here -- this is, again, framed in a cost effectiveness plane, but you can do exactly the same analysis just thinking about effectiveness. You have effectiveness on the X-axis and cost on the Y-axis. The things above

the X-axis raise costs, the things below save money, the things on the right benefit people, the things on the left harm people.

The line up in the northeast is a cost-effectiveness threshold and above that we say things are too costly even though they're beneficial, and below it we say they're cost-effective.

So, you can take a look at -- and the quadrants mean things too, so most things are up in the northeast where it costs more but it's better. On the -- in the northwest we have things that are less effective and costly. We sort of never want to do those things.

Then in the southeast we've got things that save money and make people better off. We're always going to want to do those.

The little dots, what are they? They're people. They're people who differ from each other. Some are benefitting from a treatment, some are harmed, some are saving money, some it's costing money.

What are the colors of the dots? The blue dots are people choosing the treatment. The orange dots are the people not choosing the treatment. You can see the blue dots tend to be mostly on the right. People who benefit from things tend to choose them.

But there are mistakes. So, if you look on the left side, on the west, in the northwest in particular, there's a blue dot there, someone who's choosing the treatment but actually being harmed from it. So, we want to help them. How can we help them? Help them make a better decision by not doing that.

And that's what decision aids can do, they bring the people on the west, who are making the mistakes, and bring them to stop doing it. The people on the right who should be choosing it who are orange dots, but aren't, you bring them back by getting them to stop doing it.

And then you can add up the benefits of those decisions in terms of better outcomes, in terms of saved money, and as you add those up, you

can convert them into measures of that benefit. And one of the things that Anirban and I did in this paper is calculate, for example, for prostate cancer treatment, localized prostate cancer treatment, what would it be worth for men to make -- if you could just figure out the one best treatment for all American men for localized prostate cancer versus the best individual level treatment, and the point was 100 times greater value when you can get the best treatment for the individual.

So, the individual really matters and these frameworks can be adopted to incorporate that individual value.

Now, I've talked about individualization. Let me turn to sort of this question of inclusiveness and how we think about that. So, you know, this is a harder one for VOI because what these approaches, population approaches tend to do is average over everyone, but I think there are ways in which these help. You can't maximize population health if you omit large parts of the

population. And this is especially true when the parts of the population with the greatest health problems are those that potentially are the most marginalized.

So, if you really want to improve population health, you should be focusing on these. So, I wouldn't under appreciate the value of population health.

The other thing is you can over weight the health of parity populations. You could ask, what research has the greatest VOI for particular priority populations. In your extreme you could put no weight on other populations, I'm not saying we should.

The other thing you can do is you can treat inclusiveness as a separate criterion from VOI and use judgment to weigh them against each other. So that's -- you know, there are a variety of ways you can bring this in.

So, let me just conclude. VOI provides a mechanism to estimate the population health impact of specific research questions. Although it can be

burdensome to apply their methods for its practical application, and I've described maximal modeling, full modeling, limited modeling, inceptual VOI, and there are VOI approaches to value individualization.

Now, VOI can be used in a variety of ways, and this is really key to today's discussion. It can be used to prioritize research studies, a particular study, does this matter, and areas. Now, prioritizing research studies is a lot more straightforward than prioritizing areas.

So, how do you approach areas? Well, one idea is that VOI in areas can be bounded from above. You can say there's only so much burden in this area, but I think that's not actually going to be very informative. I think what's far more likely is that the value of research in a particular area should be the function of the individual studies that you might do in that area, and this has a very important implication and that is that when PCORI goes ahead to prioritize areas, it should still be the case that studies in

prioritized areas should still meet the criteria for value, particularly at the margin.

And so one proposal I would make to PCORI is to reserve money outside its allocations to fund the most meritorious studies in areas when they run out of money in that area for what they've originally allocated. In other words, you're going to fund the very best study in every area that you've prioritized and commit to it, but then you're still going to have some good studies left over and you should keep money to do that.

So, that's one idea, so sort of finally I'll just say, the practical experience with VOI is limited but it's increasing. It exists in the UK, it's growing in the U.S. and I think that as we think about how to use this, it's critical that we integrate this in a way that compliments existing prioritization processes rather than competing with it.

So, let me stop there. So, thank you.

[Applause.]

DR. WALLACE: We will have an opportunity

for dialogue and questions after our next talk too, but we did want to also then move ahead to the next paper, which is going to be shared by Claire McKenna who worked with Karl Claxton to produce a white paper *Expected Health Benefits in Additional Evidence: Principles, Methods, and Applications*.

Claire is a research fellow with the Team for Economic Evaluation and Health Technology Assessment at the University of York, that would be Old York, not New York, and Claire has degrees, actually, in mathematics, theoretical physics, medical statistics, and health economics.

So, she'll share with us how she reconciles those various perspectives in thinking about how we can do prioritization. Claire?

MS. MCKENNA: Okay, good morning everyone, and apologies for Karl not being here due to illness. He's doing very well and he is listening in the webcast.

So, I'm going to discuss the principles and methods and show some applications of how value of information analysis that David has just

described can be used to estimate or establish the expected health benefits of additional evidence and how it can be used to prioritize research decisions.

So, the purpose is to demonstrate the principles of what assessments are required when considering the need for additional evidence and the priority of proposed research, and these assessments do reflect a number of PCORI's criteria on the impact of the condition on health, the potential for improvement in health, and the potential for improving health system performance.

And we're going to illustrate how these assessments might be informed by quantitative analysis that's based simply on standard methods of systematic review and meta-analysis.

And in doing so, we'll see that we need to carefully distinguish between the value of additional evidence and the value of actually implementing the findings of what existing research suggests.

So, these assessments will help to

establish whether a particular research proposal is potentially worthwhile, whether it should be prioritized over other research topics that could have been commissioned with the same resources.

So, we have produced this white paper that sets out what assessments are needed and how might these assessments be informed.

So, what assessments are needed? Well, we first need to establish the value of additional evidence. On balance, the existing evidence might suggest that a particular intervention is expected to be the most effective, but due to uncertainty in the evidence, there is a chance that another intervention may be more effective and could improve health outcomes to a greater extent.

And so, we need to establish how uncertain we are, how much does that uncertainty matter, and what are the consequences if we get it wrong, and these consequences represent the maximum value that we could gain from additional evidence.

And we also need to know whether the findings of research are likely to be implemented

into clinical practice. So, clearly the health benefits will only be realized if the research has an impact on clinical practice, and so if it's unlikely to be implemented, another area of research with smaller potential benefits but more likely to be realized, might be regarded as a higher priority and, in fact, the potential improvements in health outcomes by encouraging the implementation of what the existing research suggests might exceed the potential improvements from conducting additional research.

And so, the notion of a minimum clinical difference in outcomes is required. So, this is the difference in outcomes that would need to be detected between the treatments in order for the end results to have an impact on clinical practice, for the results to be considered to be clinically significant and change clinical practice. So, clinical practice is unlikely to change without that estimate of an effect size.

So, we can estimate the expected health benefits of additional evidence for a range of

minimum clinical differences and outcomes that would need to be detected. And larger differences may be required when there are other aspects of outcome that might not be captured in our primary endpoint or their significant resource system or patient cost implications.

So, we'll show how these assessments can be informed in different contexts and we're not going to directly address variability in patient outcomes and individualized care, but of course, as more sources of variability are observed, then the potential value of additional evidence falls.

So, how might these assessments be informed? Well, they can be informed through the application of value of information analysis and to standard, random, or fixed effect meta-analysis as commonly conducted as part of a systematic review. And we'll illustrate this through the application of case studies to four particular contexts which are likely to arise in research prioritization decisions.

So, firstly, where he primary endpoint in

the meta-analysis captures the key aspects of health outcomes, and we'll look at that in a cumulative meta-analysis looking at streptokinase for the treatment of acute myocardial infarction. Then consider where the primary endpoint in the meta-analysis needs to be linked to other aspects of health outcome, and we'll look at that in the case of steroids following traumatic head injury.

And then we'll consider where different weights might be applied to reflect the relevance of evidence, and we'll look at that in the case of probiotics in severe acute pancreatitis.

And then we'll consider where more than two treatment alternatives might need to be compared and we'll look at that for different chemotherapies for advanced ovarian cancer.

Okay, so where the primary end point of the meta-analysis captures the key aspects of health outcome. So, here we're looking at how evidence accumulates as a sequence of clinical trials over time. And so, this is for the use of streptokinase versus control for the treatment of

acute myocardial infarction where the primary endpoint in the meta-analysis is mortality.

So, this shows the sequence of clinical trials in a standard forest blot, and the uncertainty associated with the individual trials, and if you pooled across all these trials, the pooled estimate of effect favors streptokinase with an odds ratio of, I think, 0.76 and it is statistically significant.

So, the question here is, when might it have been reasonable to conclude that the evidence was sufficient to recommend strept, and at what point in the sequence of trials was it unlikely that additional evidence would have been worthwhile? And could health outcomes have been improved by encouraging the implementation of what the existing evidence said at that time or by acquiring the additional evidence? And how might that additional evidence that is required, be judged relative to the need for additional evidence in other clinical areas.

And we're not using hindsight to answer

any of these questions, but instead we are using the quantitative value of information analysis.

So, to your right it shows the sequence of clinical trials re-analyzed as a cumulative meta-analysis where he estimate of effect on mortality and the uncertainty is updated when each subsequent trial reports, and you can see from this that, on balance, the evidence very quickly favors streptokinase versus control, but it was not until the European III trial that we got a statistically significant result in both the cumulative meta-analysis and the individual trial.

So, in other words, where we had a 95 percent chance that strept was expected to be more effective than control, and it might mean at this point the clinical practice would have responded to the evidence.

So, this tells us something about the uncertainty in the evidence, but it doesn't tell us about the consequences of that uncertainty. And it doesn't tell us about the potential gains and health outcomes that we could gain by conducting

additional research.

So, the chance of making a wrong decision due to the uncertainty in the evidence can be translated into the consequences in number of deaths and by applying the estimate of relative risk to the baseline risk of mortality, and to an estimate of the size of the population that could potentially benefit from this information.

And so, this figure here shows the distribution of consequences of uncertainty in number of deaths at the three different time points.

So, the European I was early in the sequence of clinical trials and at that point there was a 70 percent chance of no consequences, but there was a 30 percent chance of a large number of deaths, and whereas later in this sequence of clinical trials, they were less uncertain that strept is more effective than the control, but there's still as mall chance of a large number of deaths per year.

And so, the expectation across this

distribution of consequences represents the maximum value of additional evidence, so early in the sequence at European I, the maximum value of evidence was about 6,200 deaths averted per year, whereas later in this sequence of clinical trials, then the value of evidence falls because we're less uncertain, and by European III trial, it's about 27 deaths averted per year per annum.

And while this solid black line at the bottom shows how the value of additional evidence declines with each additional study that was conducted, and you can see the tail end of that that those later trials in the sequence may not have been necessary to inform the question of whether strept was more effective than control. And, of course, then there would have been harm to patients that were enrolled in those later subsequent trials due to being enrolled in the wrong arm of the trials.

Now, as I said earlier, of course, that the evidence is only valuable if it has an impact on clinical practice and so the dash line in this

figure shows the value of switching from no strept to strept in clinical practice, and assuming that clinical practice only responded to the change at European III we noticed statistically significant results in both the cumulative evidence and the individual trial, then the value of implementing the evidence falls to zero.

Well then we can also look at the value of additional evidence and number of deaths averted per year for a minimum clinical difference in the risk of death between treatments that would need to be detected for the research to have an impact on clinical practice.

So, that's shown here at three different time points for a range of minimum clinical differences in size if we need to be detected. So, the value of additional evidence declines with the -- when you need a larger effect size to be detected because, clearly, these larger effect size are less likely to occur.

Okay, well, now I'm looking at where the primary endpoint in the meta-analysis needs to be

linked to other aspects of health outcomes. So, a good example of this is the case of steroids following traumatic head injury. So, before the CRASH Trial, that's a large, randomized control trial that was first reported in 2005, before that trial there was a large number of smaller trials looking at the effects of steroids on death and disability following traumatic head injury. And the evidence was very mixed. Before CRASH, the odds ratio of death with the use of steroids was 0.93 and you can see that the confidence interval crosses the no difference line while the odds ratio of death, vegetative, and severely disabled was 1.1 and, again, with considerable uncertainty.

So, in this case, we need to analyze all the trial evidence and all the important aspects of health outcome, which in this case were reported in terms of the Glasgow Outcome Scale disability levels, which is presented here, so we can synthesize the evidence to give the proportion of individuals that is expected to be in each of these health states by treatment.

And then to quantify the outcome of survivors, we can use estimates of life expectancy given survival and quality of life associated with these Glasgow Outcome Scale outcomes, and that will give us the equivalent years lived in full health.

So, in this example, on balance, the evidence suggests the steroid should not be used in clinical practice if you consider all aspects of health outcome, but there is considerable uncertainty in the evidence base before the CRASH Trial, so the probability of no consequences is 0.63. So, there is still a 37 percent chance of a large number of consequences in terms of lost years lived in full health per annum.

And, as I said, the expectation across this distribution of consequences is the maximum value that we would be willing to pay for additional research, which in this case is around 1,000 years of full health per annum.

So, the question here is, are those 1,000 years of full health per annum, were they sufficient to regard CRASH Trial as worthwhile, and

should it have been a priority over other research topics that could have been commissioned with the same healthcare resources?

Well, the CRASH Trial was commissioned in the year 2000 and assuming that the information would be valuable for about 15 years, then the value of -- the maximum value of the evidence would be about 15,000 years of full health, but the CRASH Trial wasn't expected to report to the year 2004, and so the value of additional evidence falls with the time it takes for the research to report, and so the value of CRASH was expected to be about 9,000 years of full health lived.

So, was the CRASH Trial worthwhile? Well, the cost of the CRASH Trial was 2.2 million pounds and in the UK, that could have been used to generate 110 years of full health or alternately you could think of in terms of the UK NHS we'd need to spend an additional 179 million pounds to generate that same improvement of about 9,000 years of full health elsewhere in the NHS.

So, in this case it did appear that CRASH

was worthwhile and there is no additional value to evidence after the CRASH Trial.

Well, now considering the use of different weights that might be used to reflect the relevance of evidence, and here we're looking at the case of probiotics in severe, acute pancreatitis. So, in this case, there was two smaller trials that showed a non-significant improvement in the risk of death with probiotics.

But then in 2008, there was a much larger trial that showed a significant increased risk of mortality with probiotics. So, this opened up a debate about the relative effectiveness of probiotics and about the relative merits of the trial evidence.

And if you pooled across the three studies in a meta-analysis, you get very different estimates of effect under a fixed and randomly fixed analysis, and you can see that there is considerable uncertainty.

So, in this case, we may need scientific value judgments about the differences between these

trials and the relevance of the evidence to clinical practice. And so, these scientific value judgments will not only change the estimate of effectiveness, but will also change the uncertainty associated with it and, hence, the value of additional evidence.

And that's illustrated here in terms of the number of deaths averted with additional evidence for a range of minimum clinical differences in the risk of death, and this is for random fixed effects analysis and you can see where we've got standard weights, but then if we increased or decreased the weight that we would apply to the two earlier trials based on some scientific value judgment of how you would weight the evidence of these three trials, you can see the impact that it has on the value of additional evidence.

Well, now all the previous examples that I've looked at have only considered two comparators, but I also wanted to just illustrate that we can also deal with situations where there

are more than two alternative interventions that need to be compared, and in this case we're looking at three second-line treatments for advanced ovarian cancer.

So, in this case there was three trials, each with a pairwise comparison, so topotecan was compared to paclitaxel in one trial and topotecan was more effective than paclitaxel, the hazard ratio was 0.91 in terms of survival.

Then in a separate trial, paclitaxel was compared to PLDH and paclitaxel was more effective with a hazard ratio of 0.91.

And then in another separate trial, PLDH was compared to topotecan and it was a much larger trial than the other two trials and PLDH was more effective than topotecan.

So, this is an example or a case where on the basis of the pairwise comparisons itself, the evidence appears inconsistent, but remember that each treatment effect is estimated with uncertainty, and so in this case we need to come to some overall assessment about the relative

effectiveness of all three treatments.

If we just considered each of the pairwise comparisons separately to try to come to some overall assessment about the three treatments, we would be implicitly breaking randomization. We don't have a trial that looks at the three treatments together.

So, we could use like an indirect treatment comparison based on a single common comparator, but in this case that would mean excluding the evidence from one of the trials because only two of the three trials have a common comparator.

So, a better approach would be to use a mixed treatment comparison that makes use of the full network of evidence, both the direct and the indirect evidence, and just to illustrate the impact that that has on the value of additional evidence, depending on how you synthesize the evidence, again this shows the value of additional evidence and number of deaths averted for a range of minimum clinical differences in the hazard of

death in this case and you can see that I've used an indirect comparison or the pairwise comparison you could substantially overestimate the value of additional evidence.

So, it illustrates the importance of the method of synthesis that you use in order to estimate the value of evidence.

Well, just to conclude, I hope I've demonstrated that quantitative analysis based on systematic review and meta-analysis does provide a practical and useful starting point for research prioritization and commissioning. It adds transparency and accountability, but of course we're not saying that it captures all scientific and social value judgments, so there's plenty of room for deliberation here. And some considerations for PCORI is whether this type of analysis could be used, whether -- who would be responsible for conducting the analysis, et cetera.

Thank you for your attention.

[Applause.]

DR. WALLACE: Well, thanks, Claire. We

have about 10 minutes for questions and discussion, and so why don't we start in the back.

MS. WILSON: I actually have some comments coming through from Dr. Karl Claxton who wanted to say first that strongly, and I hope I do these comments justice, strongly agrees with Dr. David Meltzer that should not fund all proposals that appear worthwhile as they are made, but hold back some resources to make sure that there are sufficient funds to support more valuable proposals that might be made later in the cycle.

Additionally, he supports the need for maximal or policy modeling if it is clear that it would be particularly valuable in a particular area, indicated by the sum of potential benefits across the meta-analysis of evidence relevant to specific questions in that area.

One more comment. Considering the relevant potential for bias in the evidence is very important and using a random effect is not necessarily the best thing to do as illustrated in the probiotic example.

Therefore, in the white paper, we recommend sensitivity analysis and potentially weighting trials so that the decision maker can see the implications of value of evidence of taking different views.

I believe I might get more comments from Dr. Claxton, but thank you, we wanted to prioritize his comments.

DR. WALLACE: Very nicely channeled too, so thank you. I think we had our first question back here and then we'll come up here.

PARTICIPANT: Yes, we have heard, I believe, two different approaches to the use of cost effectiveness analysis, one by Dr. Wilensky in which it should be done after by the payers rather than factored in, unless I'm misinterpreting -- factored in at the onset of prioritization, and then, of course, the two presentations just now, and where it would be done at the prioritizing at the proposal stage.

My question is for PCORI leadership, how they are -- what process they're going to use to

mediate between these two approaches.

DR. WALLACE: Well, one -- I might, just process-wise, one of the opportunities we're going to have later in the afternoon is to actually hear more directly from PCORI leadership about how they're synthesizing not only this input, but also the additional input from the experience with the process.

So, if that's acceptable, I guess my suggestion would be that we defer that question until we actually have the opportunity to talk directly with staff.

Let me -- we have a question up here and then to the back.

DR. WEISMAN: Okay, I'll --

DR. WALLACE: Again, please identify name and where you're coming from.

DR. WEISMAN: Yeah, I'm Harlan Weisman and I'm a member of the Board of Governors of PCORI and I'm not going to address the last question.

It's really a question for you, David. In your azithromycin versus augmentin example, and the

idea was if there's plentiful or at least good clinical trials information you can rely on that for some of the value of information modeling, the thing that worried me a bit, and I actually on my iPhone looked up at least one of the articles about this, and is that, you know, azithromycin is given once a day for three days and augmentin is given three times a day for ten days, and there's some real world values that may not at all have been addressed in that randomized clinical trial, and that would be true, I think, also in the CATIE trial.

So, it would seem to me that you could both underestimate and overestimate the value of information based on the difference between the clinical trial aspects, which is well controlled by definition, and what's likely to occur in a real world setting, particularly in different populations in the country.

It's very hard, for example, to get adolescents with sinusitis to take a regimen three times a day for ten days. So, I'm just wondering

about that and how do you factor that into the VOI?

DR. MELTZER: Sure, so let me just say, you know, again, it's an example of a particular application and any application has issues that you need to be concerned about.

It was a clinical trial, clinical trial population, it's certainly possible that people were more compliant in this study than they might be in another study, or in another context --

DR. WEISMAN: Or in the real world.

DR. MELTZER: -- right, presumably, though, it's just interesting if you think through the logic in this particular study that presumably, if efficacy were lower, it would make azithromycin even better, right, because augmentin would look even worse, and as a result, it would be even more clear that azithromycin were better and the value of information would be even lower.

So, this gives you a nice upper bound, even of that, but I think the general point here is let's say we had a better efficacy study, okay, the question is, do we want to do yet another efficacy

study that is larger and more precise, and that's the general approach.

DR. WEISMAN: Right, and my only point is since PCORI is not always, but will fund, more real world like studies --

DR. MELTZER: Absolutely.

DR. WEISMAN: -- that the experiences based on randomized clinical trials may not be helping us necessarily assess the value of -- or the utility of a real world study or observational study in a larger population.

DR. MELTZER: Sure.

DR. WEISMAN: You know, for example, bacterial cure, which you didn't talk about, was much higher, much quicker in the azithromycin group, which suggests that, you know, non-compliance would be a big issue.

DR. MELTZER: So, I want to be clear, though. So, there are differences between effectiveness studies and efficacy studies --

DR. WEISMAN: Right.

DR. MELTZER: -- but there's really

nothing about value of information analysis that makes it more or less suited to studying one or the other. You start with a study of a given size, it has a given level of confidence around the estimates, you are asking the question, should you do another bigger study, and this issue is a relevant issue, but it's not one that differentially advantages or disadvantages the VOI and prioritization. Does that make sense?

DR. WALLACE: So, it's perhaps fair to say, though, that there's a lot of nuance in the I variable?

DR. MELTZER: Sure. Sure, yeah, you have to think about the context in which you're studying anything and that matters.

DR. WALLACE: Great. We had another question in the back?

MS. WILSON: This is Katie Wilson again with PCORI, and this time on behalf of Dr. Michael Lauer with NHLBI. This question is for Dr. McKenna. Dr. Ioannidis, whose name I might be butchering, which I should know, has written a

meta-analysis of many small trials is more likely to yield the false positive finding as compared to a few large-scale trials. I suspect that doctors know that, maybe not explicitly, it is arguably more worthwhile to do a few large-scale trials like GISSI, which was very cheap, than lots of small trials, which won't be believed even if combined in meta-analysis.

He would be interested in hearing your thoughts. Thank you.

MS. MCKENNA: Yeah, that's absolutely true, but of course, if there's a lot of uncertainty and there's a larger trial, then obviously there would be more people enrolled into perhaps a wrong arm of the trial based on that uncertainty. So, there is a down side to having larger trials in that sense, but you're absolutely right, the larger trials will provide, hopefully, more valuable information.

But what we've presented here is the use of value of information analysis from the starting point of where the meta-analysis, the systematic

review, has been left off. Thank you.

DR. WALLACE: Let's see, in the back I think we have a couple questions at that table.

DR. LAUPACIS: So, Andreas Laupacis, University of Toronto. A question and a comment. When I looked at the CRASH and streptokinase examples, my gut feeling was that sort of seasoned researchers and health policy folks and clinicians might have actually all come up to the same conclusion you did, that the confidence limits around the benefits of streptokinase were incredibly narrow, the ones around the CRASH were wide, and people probably would have said, in the former case, not worth funding another study, in the latter case it was.

So, the question is, my sense is that this sort of detailed analysis is likely to be most useful when it's really much less certain, and then if it is much less certain, then suddenly the black box element of your analysis and all the sensitivity analysis, makes it kind of probably less believable and understandable by people.

And that leads into my comment, which is, my general sense is that this is a sort of interesting, exciting way to go, but if PCORI or any of the rest of us that do health services research want to go this way, we've got to invest a lot of effort into explaining this to patients and clinicians so they actually understand it, because without doing it, it's sort of like we want you engaged, but by the way, we're using a process that none of you can understand. Because there is a pretty big black box element to this right now.

DR. WALLACE: Comments? Reactions?

MS. MCKENNA: Well, I think that -- well, to answer one part of your question, and I think that's why we didn't just look at the value of additional evidence on the basis of uncertainty, we also looked at the value of implementing the findings into clinical practice.

In the case of the CRASH Trial, there was a lot of uncertainty. But in the UK there was still about 12 percent of people -- there was still about 12 percent utilization of steroids in

clinical practice, and without the CRASH Trial, those steroids would continue to have harmed individuals, and it was only after the CRASH Trial that people stopped using steroids.

And so that's why it's important to consider the value of implementation, getting the findings implemented into clinical practice and not just looking at the value of additional evidence.

DR. MELTZER: So, to respond to the black box comment, I'm very sympathetic to that and I think there's a tremendous need for education. There are very few researchers who really know how to do this. Even the researchers who do know how to do it, many of them have sort of areas of specialization, so they don't have a sense of the full scope.

And then, in addition, if it's going to be used, we really have to have people understand what it means. So, I know there have been discussions on the Methodology Committee about making greater education in these topics an important priority. I think that -- I hope that will be something that

happens.

I think, you know, one way to think about this meeting is that it's sort of a first start towards that, but as you can see, there's a lot of content here and it can't be condensed into two 30-minute lectures. It's going to take a real investment over time. And along the way, I mean, all of us who are doing it are going to learn a lot.

I do think the sort of conceptual value of information approach is, although not easy to apply, as we've learned, a little easier to get your head around in some sense if you're being introduced to it, but we have work to do in all these areas and it's going to have to be participatory.

DR. WALLACE: So, I think we have time for one more question. Back here -- actually, we'll take two because I know you've been patient.

MR. PUN: Yeah, I'm Ting Pun. I'm really a caregiver and a patient. Okay. This is a question for David, actually.

DR. MELTZER: It's a little hard to hear you.

MR. PUN: This is really a question for David because your comment on individual variations, it's very, very interesting, okay, but on the other hand, those can only be analyzed after a trial or something because, you know, some of the variation is really based on the issue.

So, as far as the prioritization issue is concerned, this would be more useful for looking at the briefs, writing the briefs, to really try to assess that issue where the concept of VOI, when it was introduced in the prioritization process, the concept is quite easy to grasp, and without a lot of the probability and so on and so forth.

But where would it help in this whole prioritization process, and I thought it would be useful for looking at the briefs and getting the briefs out.

DR. MELTZER: Yeah, you know, I wish I had a spectacular answer to that question. I don't feel like I do, but I have some partial answers,

which is that, obviously you can learn things about individuals sometimes based on attributes that they share with others. That's one way to do it. There's a lot of interest in the Methodology Committee about talking about estimating heterogeneity and treatment effects. Some of that can come from trials that are designed specifically to do that, such as crossover trials and [inaudible] sort of trial designs.

Other parts of it can come from observational studies sometimes and looking at the variability in individuals. Some will come from biological information. And then ultimately there are going to be limits to our ability to do that.

But the point is, you know, we don't have to treat everyone that they're exactly the same and the more we can move towards this, there's likely to be great value in understanding more about it. So, I think those are some of the things that we can do. I don't know if you want to add.

DR. WALLACE: Maybe our last question over here.

MS. HUFTLESS: Thank you. Hi. I'm Susan Huftless from Johns Hopkins University, and I'd like to really commend PCORI for looking into looking at the VOI analyses. For nerds like me, it's really an elegant way of synthesizing all the information and being able to compare it.

But my question is, if this is going to depend on previous systematic reviews, and many times from those systematic reviews, when we try to do a meta-analysis, we can't actually do a meta-analysis of the patient-important outcomes, what really matters to patients.

So, how can we bring in what matters to patients into these models from the beginning to go ahead and prioritize this information? Thank you.

DR. MELTZER: I'll give it a shot, and Claire, if you want to. I mean, this is obviously really, really hard.

MR. WALLACE: David, can you use the mic?

DR. MELTZER: I'm sorry. It's obviously a really hard problem, and I think the reality is that VOI can't be the only criterion. It's just

simply too hard to apply in every circumstance, but where you are able to apply it and where you see something either seems like it matters a whole lot or maybe doesn't matter much at all, then it forces you to think about how to incorporate that information into a broader process.

So, I guess the way I imagine this is that in the end, human beings have to make decisions, and they do it with information that they have available to them, and that information could say, you know, 1 percent of the U.S. population is affected by schizophrenia for their entire lives or that information could be you're talking about a rare disease with mild morbidity about which there's little uncertainty, and those are -- sort of putting those things together in a sort of good package seems to me useful, but it's not a substitute for human judgment, nor should the constituent parts that went into that be neglected even when you put them all together.

And so, you know, the last thing I'll just say is, in any research, there are unexpected

results you never expect, and we have to remember that if someone thought VOI should be used to prioritize all research, we'd never do basic science research again, and that would be a tremendous tragedy, right. So, I think we have to put this, like all tools, in context.

DR. WALLACE: Great. Well, please join me in thanking David and Claire for a really stimulating session.

[Applause.]

DR. WALLACE: So, we've kind of done the food for thought thing, now it's time for actually food for the body, and so we have about 45 minutes for lunch.

The directions for lunch are to go out the door and seek out the Arbor Room. The Arbor Room is sort of that way and there will be signs, actually, that will lead you there, and we have about 45 minutes for lunch.

Your other task is to talk amongst yourselves about what you've heard this morning so that this afternoon we can amp up the level of the

discussion. So, thanks, everybody, and we'll see you back in about 45 minutes.

[Whereupon, at 12:34 p.m., luncheon recess was taken.]

A F T E R N O O N S E S S I O N

[12:34 PM]

DR. WALLACE: Okay, well, again, just to review where we are in the day. This morning we thought a fair amount what the needs are, preliminary thinking about how we're going to approach them, some context around why this is important to do, and then also some scholarly work around what do we know about prioritization and what are the different ways that we can have conceptual frameworks that can help to guide prioritization.

This afternoon -- so, we've been at 20,000-30,000 feet and we're going to swoop down close to the ground this afternoon and we're going to progressively dissect where we are in terms of the experience and where we want to go in terms of thinking about prioritization going forward.

So, part of my job today is basically to introduce people who don't need any introduction, so, I will be very brief, but I think most people know Jean Slutsky. Jean is the director of the

Center For Outcomes, an evidence agency for healthcare research and quality and, you know, Jean has been a thought leader for quite a while in how we assemble evidence, how we use evidence, and how we transfer evidence into stakeholders or for stakeholders.

I would also mention that Jean is from Iowa, which is very much to her credit. If there are any other Hawkeyes in the room, that's a good thing.

So, anyway, let me turn things over to Jean and Jean will introduce the rest of the folks who are in her panel.

MS. SLUTSKY: Thanks. It's really a pleasure to be here. It's really disconcerting to know that you can see me on this screen. I'll just tell you a very quick story that I was giving a talk at the first inaugural NICE annual meeting and they brought me on the stage and they said, so, here you're going to give a talk here, and I looked and they had like a two-story video cam of the speaker. And I grabbed the AV guy by the neck and

I said, if you put my picture up there, you're dead. And he goes, well, you really are an American.

So, anyhow, it's my pleasure to be here with so many people that I've met throughout my career about this really important subject. We have a great panel. I'm only going to introduce them by the first sentence of their bio. You have everything in your book.

Our first speaker will be Bobby Dubois, who's the chief science officer at the National Pharmaceutical Council. Our second speaker will be Ronnie Goff, who is vice president of the National Business Group on Health, and Sally Morton, who is professor and chair of the Department of Biostatistics at the University of Pittsburgh.

I just wanted to frame this session with a few comments of my own. I, as Paul said, I've been leading the comparative effectiveness research work at AHRQ since we were authorized under the Medicare Modernization Act, and probably one of the most challenging and interesting things that I've had to

do is to develop a program on prioritization.

I like to think of AHRQ as a learning healthcare system, a learning healthcare organization, where we plow back into what we do the lessons we've learned, and one of the things that we've really learned is that we can make investments in the methods and then apply those methods and learn from that application.

So, just sort of, I guess, a conflict of interest declaration. We have funded, as an agency, a lot of value of information work, both Duke University and Dave Meltzer at the University of Chicago, but we've also taken a new look at the role of systematic review and you heard that at the last session that systematic review can be a very powerful tool for a lot of things, both dissemination, but also identifying research gaps.

What it can't do is necessarily prioritize those gaps, so we've actually made a big investment under the ARRA funds to develop about 50 future research needs articles that were based on stakeholder-driven panels, and when I say

stakeholders, I mean really stakeholders, so not only patients and caregivers, but researchers, funding agencies, health plan administrators, people who actually have the condition under study, to look at the research gaps, help to prioritize those gaps that are needed for information, not just innovation.

So, it's been a really interesting process that we're in the period now of looking back at it and trying to identify how well it's worked and how well it's working, and I feel that this is a young field, but it's also a field that has some of the best minds in health services research that are taking part in it.

Sally has promised, as a biostatistician, that she has no formulas in her slides. And David, maybe one or two of your slides should be reworked just because it's after lunch and formulas are kind of icky.

So, we'll leave it at that, and I want to leave time for questions at the end, so we're going to try to stop at about 1:10, so think of your

questions. This is a great opportunity to ask us what we think about research prioritization.

So, Bobby?

DR. DUBOIS: Thank you. Okay. Thank you for giving me an opportunity to be here. Let me just being by saying you guys are doing a lot of things right, so before I suggest some things to think about, just to underscore, there's no sense worrying about prioritization if you don't have a good list of questions to start with, and so you guys have a great process for getting the questions, so that's the first thing.

I think you've got many ways of bringing the questions to the surface and I strongly support everything you're doing in that regard. You have criteria for prioritization, you've got goals towards transparency, you've got a lot of different things. So, lots of the stuff is really excellent.

What I'd like to do is in the next six minutes, is to give you six things to think about, one per minute. The first is, a lot of the prioritization results will be dependent upon the

weights you attach to the criteria. Is it more important to deal with diseases that are highly burdensome, or projects that are implementable, et cetera, et cetera? Who's going to derive those weights? I suggest it should be the Board and they should be transparent, up front, so everybody knows. So, that's the first thing.

Secondly, you guys want to be transparent, but I think it will be important to, when you have your 400 or 500 questions, how did you get down to 100 questions, how did you get down to 50 questions and whatever the final number is? Like a grant submission process, it would be good for the question submitter to get the weights -- or not the weights, but how you guys ranked them on all the five things that they were evaluated based on because maybe they can resubmit the question, just like a grant, and tweak some of it to make it more relevant.

Third, you should test the reliability of the process. So, if you have multiple different groups making some of these choices, if the

membership of the groups evolves over time, it would be useful to do test reliability. You learned in the two groups thus far that there is variability. So, we need to understand that variability, and to the extent we don't want it, if we don't want it, then work on it.

Fourth, this has to be industrial strength, you know, making of sausages. The problem is, it's one thing to do this with 20 questions, develop 20 briefs, but you've got 400 and that's very quickly going to come to 800 or 900. You can't do this whole process with 900, as Rachael and I chatted over lunch, you'll winnow it down probably quickly to a manageable number, but that winnowing process has its own process and transparency, and probably would be done by staff and creates a whole set of problems. So, probably it's time to think about and begin to share what that would look like.

Five, I think it's important when you're prioritizing to think about cost, and I don't think about costs in the other ways, cost to do the

study, because when I was participating in this, if I knew -- this is a really cool research question, but it's going to take 80 percent of the PCORI budget, this is not quite as cool a question, but, you know, we can bang it out quickly, it's not that expensive, oh, wow, that's important.

So, somehow that shouldn't just be later that we'll worry about costs because I think it does, for me, anyways, adjust how I would prioritize if I knew it was quick and cheap, didn't have to do a randomized control trial that took 22 years. So, some of those -- and when I say cost, it's cost -- time cost as well as the other.

And then the last is something, which I might call meta prioritization. So, there's some high level things that you guys have already decided, there are five areas to focus on, disparities, et cetera, et cetera, and you have some allocations across that. So, that's important to get that out there.

Joe alluded to the shift from investigator-initiated to stakeholder-initiated,

and that percentage of where it is today and where you'd like it to be, I think should be transparent and out there and the Board should decide what that is. And it can evolve over time, but whatever it is, at any one point in time, it ought to be something that, from a meta prioritization, is out there.

There are things like, how much money do I spend on common diseases versus rare diseases? That is a meta prioritization issue that the Board, I think, should probably help us to understand.

So, I think those are the things I wanted to focus on. I got it done in five minutes, and I give two minutes to the next person.

MS. SLUTSKY: Okay, two minutes has been to Ronnie.

MS. GOFF: Robert's rules. And hopefully we'll just keep passing it along. Good afternoon, everybody, it's really a pleasure to be here.

I'm going to spend about 30 seconds giving you a perspective -- or telling you who it is that I am representing, and then we were asked to talk a

little bit about reactions to the process that you're using, why we come to our comments the way we do, and what would help make this successful. So, we're going to do that in five minutes.

I am with the National Business Group on Health. We have been around since 1974. We represent the largest employers in the country. We've been working with Larry Becker for a million years and Xerox. We have about 357 members, including 78 of the Fortune 100, who buy healthcare for about 55 million people. So, they have a big stake in all healthcare issues, including this very big issue of PCORI.

We've been very interested in this area of comparative effectiveness research for a number of years now. Since 2004, we've had a committee called our National Committee on Evidence-Based Benefit Design, and that consists of employers, health plans, Jean joins us on that committee, we have medical societies, researchers, it's really a mixed group, and they came together in 2004 because employers felt there were enough healthcare

interventions out there that would benefit from better application of the science.

And so, what we've done over the years with them, and it was really a goldmine to us when the effective healthcare program started at AHRQ, and we actually had some great comparative research to use, but we worked with them to translate things from effective healthcare programs, we used Cochrane Clinical Evidence, we used a lot of the most respected sources of systematic reviews, and we say, well, if this is what the evidence is telling us, then you can use your levers as an employer and it might be plan design, some of the things that we talked about in the session with Gail Wilensky this morning, it might be purchasing as another lever.

For instance, we're starting to see a lot of employers narrowing the network of systems who can actually deliver babies because we're looking for the best providers in terms of, you know, no early induction of labor, reasonable C-section rate, things like that, so you might use that

evidence in your purchasing practice. And most importantly, they're using it to develop tools and resources to support employees and the other beneficiaries to make smart choices.

So, we've been at that since 2004 and I will say that one of the things that will be important for PCORI is to get out there early, especially now that employers are starting to pay a little bit for this, with some actionable results, because I think, as we've looked at the comparative effectiveness research, there are a lot of good things that we're learning. We've used the autism, prostate cancer, I mean, we probably have 20 or so reports out there right now. So, there are a lot of usable things.

There are also a lot of inconclusive evidence and I think a lot of talk about, well, you know, the science hasn't been that good.

So, in terms of your priorities that were laid out this morning, I just want to affirm that we think that you're right on, and in particular we would say, don't under value communication and

dissemination research, because that translation, the thing that we've been doing for employers over the years, in taking the results and saying, this is what it means for you, is so important for every stakeholder group. So, we would emphasize that.

The other point in looking over the paper in terms of the criteria, the one criterion that gave us a little bit of pause was the fourth one where you point to the -- how likely is it that the finding will be implemented and practiced? And we would say, to the extent that you think the barrier is related to some perverse incentive we have in the health system, say, around payment, don't stop, you know, don't do the research that you think is warranted because, you know, the payment system would encourage people to go a different way.

So, that was the one I wanted to comment on. We want you to be fearless in that.

And then just to reiterate what I said this morning when Gail Wilensky was up here, plan design is a tool that we can use to encourage the appropriate care based on what we find out with the

research, but it's a very blunt instrument and employers, I think, want to use that as a last resort.

We're also part of the Choosing Wisely campaign, which we love because it comes out of ABIM and it's driven by the medical community, and that's what we like to see, that the medical community is on the frontline of looking at what works and what doesn't and making recommendations around that.

So, efforts like Choosing Wisely and then also, I was just talking with Larry about this, there are a lot of efforts right now in the private sector to do transparency tools for consumers, transparency of price as well as quality, and we're going to see that continue in the next few years, so we think we have good vehicles that we can actually plug the information in that the research will give us to help people make good decisions both based on, you know, based on the science, but also based on their personal preference.

So, I think I did maybe, Bobby, use most

of your two minutes you gave me, but we really appreciate being a part of this process. Thank you.

[Applause.]

MS. MORTON: Thank you very much. It's a pleasure and an honor to contribute to PCORI's mission today. I am a statistician. When I thought about the question that I was asked to consider, how can PCORI prioritize topics, this approach or process based on the eight part PCORI criteria, the first thing I did was reacquaint myself with PCORI's mission. And as Bobby said, you're really to be congratulated for keeping that mission front and center in this process, to find research guided by patients, caregivers, and other stakeholders.

As I looked through the material, there were several words that came to the forefront, they were words like fairness, inclusiveness, trustworthiness, and I've listed them there in two columns, the column on the left I'll call "inherent attributes" and the column on the right I'll call

"extrinsic attributes" and now I'll make a couple of suggestions about how you might achieve those attributes.

So, if we look at inherent objectives, those are permanent, they're inseparable from the process itself. I think transparency, as you've heard from a lot of folks, is going to be the key to the credibility of this process. You're going to have to have a process where people feel they can answer the questions that I've listed on that slide.

Today we're focused on the last question, how does prioritization take place? But anybody looking at the PCORI process has to feel that they can answer those questions.

I think you have to think about simplicity in your approach. A remark was made this morning from the back about a black box, but simplicity is difficult. You can have a very simple process. I served on the IOM committee that sets CER priorities, and we used one of the approaches that was used by the pilot group here.

We were given a set number of points and asked to allocate them across possible topics. That's a very simple approach. We had over 100 topics to prioritize, but it can be though to be very subjective.

If you go the other direction and you have a very complex process, it's hard to explain, you might feel that you can manipulate it, I think speakers have alluded to this before, if I change the weight slightly I can move toward a topic that I really want to have research done on.

So, PCORI's going to face this kind of balance between simplicity, but I would err on the side of simplicity.

So, kind of advice that I have, and it's already been echoed here, to achieve these inherent objectives of fairness, trustworthiness, and so on, first, I would advocate for the release of the data. Bobby's already said this. I think you need to be able to report back what the raters did rate those attributes on.

You may mask the identification of the

members of the committee, but I think you have to report back.

The topic briefs are extremely challenging. How do you produce them in a common language with common statistical metrics? What do we mean by burden of disease? The challenge is, if you knew all of this about the topics, you wouldn't be doing the research, so somehow you've got to get at these topics, briefs, and this is not an easy task.

My last bullet or main bullet is actually out of date now. PCORI's already done what I was going to advise. When I looked at eight criteria I thought, oh, my goodness, this is a lot. Is there some way you could collapse? And PCORI has already done this by collapsing to five criteria. So, I think I'll move forward from there.

So then when I think about extrinsic processes as part of this approach, I really mean the things that will make it operational, and here I'm talking about things like scalability, which Bobby alluded to as can you do this industrial

strength. It was hard enough for ten topics, how do you do it for 100, and how do you do it in an ongoing process?

So, for example, if you rate 100 topics next year and 50 are discarded, 20 are moved to research, and 30 are kind of on the table but haven't reached the research level yet. When you rate another 100, what happens to those 30? Do you re-rate them or do you use the ratings you already have?

Can urgent topics, so if there's suddenly a new technology, how does it enter the queue? Can that happen quickly or do you have to wait for the next rating? Is the approach scalable? I'd like to advocate that PCORI integrate kind of a continual quality improvement perspective in the process. And there is this issue of topic balance and I think that's supposed to happen at the Board of Governors level, but I would advocate that has to be very transparent as well.

So, now I have some precise, and it's rather statistical advice, again, the first bullet

has already been said. I would argue you have to understand the reliability of this approach. So, there's kind of an inconsistency here. We're talking about individual patients'' voices, and they are raters, and they are important as individuals, but there's also a generalizability, if a different patient or stakeholder or research was doing the rating, would the ratings change? And I think the answer is, they would. And you need to understand how much they would change and how that might impact your prioritization.

I don't have an equation. You actually have to do it in your head for my second bullet. So, I think you have to incorporate the variability in the ratings.

So, let's take an example. Let's suppose we have nine raters and they're rating topic A, and we're doing a very simple rating approach, you're given a set number of points, and all of our nine raters give that topic A 15 points. So, we have a 15, 15, 15, 15 for all of our nine raters.

If you take the average, the simple

average, it's 15.

Now, let's imagine you have a second topic, topic B, and now our raters really vary. We have three raters that give that topic a zero, shouldn't move forward for research. We have three raters that give it the same rating as they did for Topic A, 15, 15, 15. Now we have three more raters, very simple example, you know what comes next, they give it a 30, 30, a 30. Again, the average is 15, but I think you would agree that these topics have very different variability in how the raters feel about the need for research to be done.

So, I think you have to take that variability into your approach. Thank you.

[Applause.]

MS. SLUTSKY: We have lots of time for questions and answers, so I invite the audience, and especially the experts who may have some thoughts to offer who aren't actually up here, to comment on the topics that you heard today.

Yes, and if you could identify yourself if

you haven't already done so previously.

MR. CHERKIN: Dan Cherkin, Seattle. I've been following this process of PCORI's efforts to really build a foundation to move on, and I think nobody could accuse them of not being fairly thorough and diligent, and I see there's a tension between trying to be overly precise and cautious and actually getting anything done. There's a lot of messiness in this no matter what way you do it. Some approaches tend to be more ostensibly precise and, you know, accurate, but in fact, the way they're used, may not be.

So, I'm just wondering if the panelists can kind of comment on, sure, in an ideal situation with years to kind of go through all of this, we could come up with a pretty cute or refined approach to ranking/rating things. But given that we need to move on, that there's really, from our experience with the panel, there wasn't a huge amount of difference amongst many of the things that we rated, and the differences were probably artificially of little clinical importance, if you

will.

So, how can we -- how can PCORI kind of move forward with transparency and scientific rigor, without getting mired in it?

MS. SLUTSKY: So, why don't -- I think this is something that each of you should address.

DR. DUBOIS: Yeah, I'm not sure I have the right answer here. I know I've chatted with PCORI a bit about this issue. Are these juries or grand juries? You know, a jury is an untrained group of people who come together on one occasion and they do whatever they need to do, vote on, you know, a trial.

A grand jury are people that are impounded for a period of a year, at least in California, I think, and they get some training and they work on the stuff over and over again, and they spend a lot of time, it's not like, well, we fly in three times a year, I mean, they spend a lot of time. So, one way to speed things up is to have more of a grand jury approach and really ask people not just to come in three or four times a year, but, you know,

really, this is a half time job or whatever it is. That's one way to speed up the process.

Then, of course, you have a smaller number of people and people then will argue it's not necessarily representative, so, you know, you're not going to win on this one.

I think also, and you guys are already there, you already identified three projects you want to do anyways, you know, and the three projects, I don't even know what they are, but I can't imagine anybody's going to argue because these are common projects that everybody cares about.

So, you know, there's the IOM 100. I think you can get started on certain things pretty quickly and, yeah, somebody will whine and say, you didn't do my one, but in the grand scheme of things, everybody wants to -- and I think you said one of them is uterine fibroids is an important one, people aren't going to argue too much.

MS. GOFF: I'm not a scientist or, you know, often involved with a process like this, but

something we say a lot in working with employers in the private sector is, don't let the perfect get in the way of the good.

So, to the extent we have low-hanging fruit, like Bobby was saying, that things where everybody can agree on, push ahead would be our advice and then you can always go back and continue to clean up the process or, you know, pick up the pieces.

MS. MORTON: I think my experience is much the same in this, that some topics seem very clearly distinct from the others, so it's almost like a dichotomous space, a binary space, you almost want a level of precision that is impossible in this setting, and we can get so mired down in the weeds we don't see the big pictures. That's why I argue not to make it too complex with a whole series of weights.

I mean, we may need weights on certain very key dimensions, which maybe within that five, two or three, but beyond that I wouldn't make it more complex than that, kind of alluding to your

point, I think, Bobby.

MS. SLUTSKY: Yeah, and I might just take a moderator's privilege here, not that I ever do things like this, but, you know, I think that that's a really good point, when is complexity warranted and when is a simpler process warranted.

Any other -- yes, Scott.

MR. RAMSEY: Hi. Scott Ramsey from the Fred Hutchinson Cancer Center in Seattle. I don't think every questioner will be from Seattle, but we'll have a couple here.

I wanted to bring up a topic that in my world of cancer is a real topic, but is often not discussed explicitly in prioritization and that's the issue that trials often fail, and I don't mean fail in the sense that they're negative, I mean fail in the sense that they don't get completed, and they cannot be completed for a variety of reasons -- the technology can change and patients can stop enrolling in the trials, there are toxicities or problems with implementing the treatment can happen in a way that wasn't

anticipated such that the participants in the trial decide they just can't go forward.

My question to you is whether that issue should be explicitly considered in the prioritization criteria or whether PCORI should just simply accept the fact that some of the studies that they're going to undertake are going to not be able to be completed for a variety of reasons? And I think it's a real risk because you're talking about studies that are going to be conducted in very messy delivery system settings as opposed to pristine, controlled clinical environments.

DR. DUBOIS: Well, I can start. I took that factor into account, actually, when I looked at the issue of reduction of uncertainty, you know, can we actually pull off a study that will reduce uncertainty, which to me takes into the factor of, this is too big a study, it's going to fall apart for any of a number of reasons.

But I think you're touching upon a really interesting topic, which is, I mentioned that you

should probably say costs, so how much is it going to cost me to do this one. I think you should also a priori be thinking about how many studies need to get done in each question, because my belief in the work we've done is that, you know, you publish a study, it doesn't necessarily change practice, you publish five studies on bone marrow transplant and release them at the same ASCA meeting, you change practice.

So, I think there's something that also -- and whether that's the prioritization people that have to do this or some other group, I don't know, but I think it's another piece of this puzzle of how you allocate your money, because if you think I can do one study in each area and spend my money, and then you realize, oh, my god, I've really got to do five studies in this area, two in this one, and one, you're going to reallocate your money differently.

MS. MORTON: I was very interested in the value of information talks by David and Claire. I'm wondering whether that sort of question, and

I'm not an expert at all in it, David and Claire, but the question is, when you think about the value of information, do you often think of it not just in the context of a single study being done but in this role of several studies being done? So, maybe it's possible to take your point into consideration in the value of information approach.

And I also think that your point about studies failing, that would be another reason to keep some of the budget aside to respond in the way that I think Dr. Meltzer suggested and others did this morning.

MS. SLUTSKY: Other comments and questions? Okay, woman in dark in the back?

MS. MUKAMEL: Dana Mukamel from UC Irvine. And just to continue on that same point in terms of the value of information, oftentimes in these randomized trials, one can design a more efficient trial by including a Bayesian approach where we don't a priority side on the sample size, but determine it as we go along depending -- adjusting it according to the effect size that we determine.

So, this might be -- we might be able to build this into the consideration of the value of the information, perhaps, and be more efficient in terms of the use of resources of PCORI.

MS. SLUTSKY: There was a woman back there.

MS. GOFF: Can I -- and maybe not exactly right on, but I think just generally what I want to say in response to that is that employers would like us to do our best to get everything we can -- all the information we can out of everyday healthcare interactions. I mean, clearly, we're starting to have the technology to do that and we see it changing from, you know, what kind of information, there's a lot of observational stuff that actually comes in, and, again, I'm not pretending to really know this area, but I would just encourage us to continue to look at methods that glean information from the everyday interactions of the healthcare system.

MS. SLUTSKY: Yes.

MS. MORTON: I would also say, in looking

at the PCORI Methodology Report, the inclusion of adaptive designs of the sort you speak of, I think, is very much on the table at PCORI. I don't mean to speak for -- Joe's nodding his head, so I think that's a great contribution to remind us of.

MS. AUGUSTINE: Hi. Erika Augustine from the University of Rochester. I'd like to ask the panelists for their thoughts about the research prioritization process as it relates to rare disease. You know, certainly as we think about impact, as we think about durability, these are issues that are all the more challenging in rare disease where we have a very small sample. Yet when we take rare diseases collectively, they do affect a large portion of the population, but any one study is going to really be specific to a fairly small number of individuals.

So, how do we prioritize research when we, in the same process, compare something like coronary artery disease to a rare disease that may affect 500 or even just 2,000 individuals in the U.S.? And so what are some concrete ways that we

can try to address that in this process?

DR. DUBOIS: Well, I guess the point I raised about the meta prioritization gets at that because, you know, if you have 500 kids and they all die at the age of two and you multiply that by a loss of 70 years times 500, you know, you're never going to get to the realm of these other diseases, which is why I think the Board needs to say, you know, we're going to set aside a pot of, you know, $12 million in this next cycle for rare diseases, and the only questions we're going to look at are rare disease questions and we'll prioritize among those.

I don't see any other way around it because even if it's highly implementable, the data would be durable, we could really, really answer this question, they'll lose on the impact no matter what you do.

MS. SLUTSKY: Yeah, and I also think it's important to look at impact on a specific population that may be greater than the population as a whole. That's another way of justification.

Andreas -- okay. Okay.

MS. GOFF: So, I'll comment then too.

MS. SLUTSKY: Okay.

MS. GOFF: Yeah, take the most uninformed person on the panel and give them a microphone and you're always in trouble, but, you know, one of the things that, again, speaking from employers' point of view, I mean, they pay for healthcare for whatever it is, whether it's rare disease or not. One of the things that I guess we'd like to see as a consideration is, you know, if it's unique, no one else is doing that work, then somebody ought to be doing it and, you know, we want to maybe make that a priority if it's not being done elsewhere versus if you have a lot of research on something. But I just throw that out there as a consideration. It's of interest to the employers, even if it's a rare disease.

DR. MELTZER: So, this is David. I just wanted to add a comment about rare diseases from the perspective of a study we've been trying to do in Chicago, and the comment is that once you start

to think about patient-centered outcomes, that often what seem to be common diseases are actually rare, and so here's the example.

We've been looking at alternative transfusion strategies to treat anemia among hospitalized older patients. Sounds pretty common, right? So, it turns out when you actually look hard at this, well, what's the patient-centered outcome we're interested in? Ambulation. In fact, to be a little more precise, the ability to report problems in ambulation.

So, all the sudden you take out older people who can't walk and you take out older people who have trouble reporting their functional status, and all of the sudden what seems like this absolutely immense group of people is actually a lot smaller than you thought it was.

And so, my comment is that the difference between rare and not so rare diseases really defines -- is defined very much by how you pose the problem, and I think one of the nice things about quantitative approaches to looking at the value of

research is that it sort of helps you put it all in a common framework that lets you weigh those things against each other.

MS. SLUTSKY: Thank you. Andreas?

DR. LAUPACIS: The question about rare diseases and how many studies should be done sort of raised to me the question of what the link between -- is between PCORI and other research granting agencies in other countries. So, for example, with rare diseases, one approach to the small sample size problem -- you'll never solve it, but it would help a bit -- would be to design studies that are funded in four or five other countries because there would be a larger number of patients. Conversely, with coronary artery disease, if another country is doing much the study that you were thinking you might want to do because it was higher in the prioritization process, I would suggest that -- and it was appropriately powered, et cetera, maybe that would make you think, well, I'm going to do a study in coronary disease but slightly different so it will

complement the research that I'm getting.

So, longwinded question to sort of ask what the -- whether there is a plan for any link with funding agencies in other countries.

MS. SLUTSKY: I might throw that question out to some of the PCORI leadership that's here to see if they want to answer that.

DR. SELBY: Jean, I'm not sure what part of it -- I mean, I can only agree with what Andreas said. Is there something special about coming from another country that you thought we should --

MS. SLUTSKY: No, I just -- I think, if I interpreted Andreas' question is, is PCORI thinking of partnering with other countries that may be doing a study that is analogous to something PCORI wants to do. So, I think his point was, and I would never attempt to put words in your mouth, so please tell me if I'm wrong, that when you're dealing with rare diseases and there may not be enough of a patient sample in any one country, that if four or five countries decide to pool resources to get a larger patient sample, I think his

question was, would PCORI entertain that as a possible model?

DR. SELBY: Sure. The answer is certainly. We are really very interested in making a contribution to the study of rare diseases. I liked Bobby's suggestion. I also really liked Ronnie's suggestion that, you know, look around. One of the things this committee is going to have to be cognizant of as it makes prioritization decisions is what else is going on.

But in answer to your question about rare diseases, yes, that sounds very attractive.

MS. SLUTSKY: Yeah, I didn't meant to put you on the spot. I just didn't feel like I could say, yeah, that sounds like a great idea with no authority.

DR. SELBY: Thank you.

MS. SLUTSKY: Other questions? Well, I think that one of the things that I would like to hear a little bit more about, and I would also invite David and other folks to comment on, how do you determine when to use a really complex

prioritization model versus when does a less complex model suit the needs of PCORI and any other organization?

So, what's the best way of determining that sort of trigger point for when you really go for the gold or where you are less willing to put a very complex modeling process in order? And I know Evan's here too, he might want to comment on that.

DR. MELTZER: [Off microphone] -- the project that we developed, which was, if you get to an answer easily, get to it easily. So, if the concept, things like conceptual value of information tell you, this just isn't going to be important, you're kind of done, and that's a good place to start.

So, then you work through other cheap methods to try to answer the question, and if they don't work, you're left with expensive methods. And then, when you're left with an expensive method, the question is, should you use another method, which is to just go ahead without spending all those resources.

And I think the answer is that if the study itself is very expensive -- well, let's do it the other way, if the study is very cheap, you just go ahead and do the study because you're not going to spend more money trying to figure out whether to do the study than just doing it.

On the other hand, if it's really, really bit, then it's worth spending a whole lot of money. So, I was asking Joe over lunch sort of how big, you know, the studies PCORI has funded are and it sounds like, you know, PCORI is just about to move into the range where it's beginning to spend, you know, a couple million dollars, not many millions, but a couple, like two, and that's moderately big, but there may be a day when PCORI is thinking like NIH and AHRQ have, spending many, many millions of dollars, and I would say in those instances you really want to try to make some investments up front to really figure out if something is worthwhile.

The big challenge, as I see it, is that those investments to figure out if something is

worthwhile often take some time and so, I mean, the discussion we were having was, you know, how do you get ahead of the topics enough so that when you're making a decision about doing something, you've got enough time to make a reasonable decision, and I think the answer is you generate many more topics than you can fund and you start the prioritization process, you know, as early as possible so you can try to do that.

So, I guess that's my thinking on it.

MS. SLUTSKY: Yeah, so, can I just ask a question that sort of feeds into that in my opinion is the question about duplication versus replication? So, could these methods be appropriate for determining when you don't want to duplicate a finding that you feel is robust enough but replicating a finding leads to important reassurance or trustworthiness?

DR. MELTZER: Well, I mean, I think that's sort of what we heard from Claire in a lot of ways. You know, how likely is it that a new study will give us a different result? And that depends

partially on what you believe about how big the studies you have so far, how confident the results are, and what your beliefs are about how comparable the settings in which they were done are so that you know, for example, whether to choose a fixed or random effects model.

So, I mean, I think those are some of the techniques that we can use. I thought it was a wonderful presentation and great study that give us hints about how to do that and I hope we'll do a lot of those things.

MS. SLUTSKY: Evan, did you have your hand up?

PARTICIPANT: Yeah. One of the approaches that I've taken, primarily because I worked within one clinical area is when we are asked to build a model, I try to think of potential future uses, and take the opportunity to imagine a meta model that I can use for subsequent work.

As you know, I'm still getting funded off of the cervical cancer model that I worked on as Jean was a young project officer at AHRQ, so that

is another approach, is to build a library of models that can be used as issues come up.

MS. SLUTSKY: Great. Thank you. Harlan, and then I have another question that I'd like to throw out before we run out of time.

DR. WEISMAN: Another -- Harlan Weisman, Board member of PCORI.

MS. SLUTSKY: Can you hold the mic a little closer for those of us over 50.

DR. WEISMAN: Yeah. You know, I've been reviewing the various criteria and I apologize, I was out of the room for about half an hour for a phone call, so if you covered it, just tell me to shut up, but there's another aspect to what we're doing at PCORI that has to be taken into account, I believe, in what we, in our research agenda and prioritization, and that is that all of PCORI is a research project, and that is patient-centered outcomes research is something that we have defined, we have characterized it, and we've got the hypothesis that it will lead to important changes in the -- in how healthcare decisions are

made and the quality of those decisions leading to improvement and outcomes of people, the American public, and that involves a lot of things including patient-centeredness, but not just patient-centeredness in that we want to do what's interesting to patients, that we want to be inclusive of patients, and that, you know, we're saying each of the research projects, specific research programs -- sorry, research grants for a study and also research areas have that in mind.

But that is a hypothesis that we are entertaining is by no means a priori true, although it intuitively feels good to a lot of people, and I think we have to be cognizant as we move forward that we are not only gathering individual research results in areas that we've prioritized that hopefully produce meaningful results, but that the fact that we did that prioritization and we did that funding resulted in something that if not for PCORI would not have been done because of the way we've chosen to go about doing things, the nature of the way we do research.

That means we've got to measure that, we've got to be able to answer the question that we made a difference, not because we had more money, and we added to what AHRQ is doing or NIH or any other funding body, because anybody could fund various disease areas or various questions, but they're not funding it the way we're choosing to do it. And therefore, an important -- to me, in priority considerations is this underlying supposition that we have to keep in mind. We can't choose something and not be able to learn from it, just the question at hand from a research basis, but we -- it has to be part of the growing evidence that we're acquiring that what we're doing is right and that we are learning along the way and adjusting and somehow we've got to take that into account, although we don't really articulate that in any way.

MS. SLUTSKY: So, that actually feeds into a question that I'd like to hear from the panel and those of you out in the audience is, I've heard that as a result of PCORI outreach that they've

received hundreds, probably close to a thousand, if it's that many, research suggestions that have been nominated.

So, my question is, how do you -- and I'm using a term that we used at AHRQ when we were deluged with topic nominations -- is how can PCORI do an initial sift and sort? Because, you know, you can't go through an intensive process on every single thousand topics in, you know, a reasonable period of time. So, what are some mechanisms that PCORI might want to try to employ to go through those thousand topics?

And I'd be interested in what the panelists think about this and some folks out in the audience.

DR. DUBOIS: Well, two thoughts, I mean, and that's part of the industrial strength question. You either come up with a lot of panels and a lot of AHRQ money to do all these briefing documents or you've got to narrow it --

MS. SLUTSKY: So, wait, did you say AHRQ money?

DR. DUBOIS: Yeah, exactly.

MS. SLUTSKY: No, no, no.

DR. DUBOIS: Money for AHRQ -- money for AHRQ to do all these, or you have to narrow it down quickly. Now, how could you narrow it down quickly? The standard approach is the staff does it, you know, that's sort of one approach to do it, and then you have to figure out kind of what does that look like.

Another way you potentially could do it is you could have domain advisory panels, you know, all of these cardiovascular questions go to our cardiovascular panel, who don't need briefing documents because they know this area, you've got patient groups that are part of the cardiac committee -- community, and they do the narrowing and they use basically the criteria, but they don't go through a huge voting process and they don't need -- you don't need to develop the briefing documents.

And then the respiratory group deals with the respiratory, and that would be another way, an

extra outside of PCORI way that you might approach it.

MS. MORTON: In the IOM experience, which did the same thing, it had a website and you could go on and nominate topics, we found that topics, many were duplicative first, second, they tended to not be stated in a way that could be easily transformed into a research idea, so I regret that I haven't looked at your form online right now for elicitation of topics, but the better you can kind of formalize those topics coming in so you can quickly do this weeding, it will help you.

On the other hand, you have to do that in such a way that it doesn't disenfranchise people, you don't use words that are difficult for people that aren't working in this space. So, that's what I would argue, try to make those topics coming in as clear -- as similar as you can too, but I agree that the kind of clinical area subcommittees might work for the first winnowing.

MS. SLUTSKY: Gail Hunt.

MS. HUNT: Gail Hunt, I'm also a member of

the Board. I had the exact same question that you had, Jean, and I was going to wait until the next panel to ask it, but actually I'd like to say beyond that.

So, you've got the 1,000 responses that have come in. They are not -- a lot of them, especially the ones that maybe came in over the transom in the Internet site -- are not going to be stated in a real research fashion, but even once you get beyond that, you've got them at all different levels. And doesn't PCORI have to sort of decide at the beginning, what's the level of what we're talking about so that we're sort of looking at apples-to-apples?

In particular, yesterday, when we had our breakout session, there were people who were making suggestions like, PCORI really needs to do research around care coordination across patients moving from one setting to another, hospital to home or, you know, that kind of thing.

And then you'd have other people that were, what I would say, really in the weeds with a

very specific topic that they were interested in, but even beyond -- it's not like it was a rare disease, it was like just an incredibly specific topic.

So, how should we be thinking about -- and because we don't have the option right now of having people come -- we've got these 1,000, we don't have the option yet of having expert panels that we can send the stuff to, the cardiology panel and all, so the staff, I'm sure is going to do this -- how do they compare apples to apples? What's the level of project that -- research project that we're looking for?

MS. SLUTSKY: So, we have one minute and 54 seconds to answer this question or to defer it.

DR. DUBOIS: I'll take 30 seconds. I think it's one of the meta issues that the Board needs to decide. I don't think there's a right or a wrong. They should all be general questions, they should all be specific. I think the Board needs to look at a family of ones and say, you know, for this year let's do 50 percent kind of

general clinical questions and 50 percent in the weeds questions or whatever it is. I think it's a Board prioritization issue.

MS. GOFF: I'm not sure who's -- at which level you'd take care of that, but something that I think are in your criteria that should come into play is; how actionable is it? If it is actionable, it may go up a step in your priority.

MS. SLUTSKY: Please join me in thanking the panel.

[Applause.]

DR. WALLACE: Okay, I think we've had a very rich discussion and several presentations about the theory about what we should be doing in terms of prioritization. I think there's also a good reminder that at some point it's good to actually do a little bit of field research about how theory actually finds its way into practice.

And so we have the opportunity, actually, now to hear the firsthand experience of some of -- I guess they would really actually be alpha testers of the prioritization scheme that's been brought

forward. And I think that as we think about subsequent iterations, it's really going to be critical for us to build on the experience of the initial explorers in this area on the behalf of PCORI.

So, I'll very briefly introduce the panel, but what I would also ask the panel to do, they're going to share with us some thoughts about their experience with the prioritization exercise, but to go back to Rachael's earliest slide, I'd also like them to share with us how they self-identify as a stakeholder so that we can hear, really, in their words about how they think about their perspective.

So, to very briefly introduce the panel, and, again, reminding you that their bios are available to you, our first speaker will be Fouza Yusuf, who is the program coordinator for the Center for Clinical Effectiveness Research at Children's Research Institute at Children's Hospital of Wisconsin and the Medical College of Wisconsin.

Next to Fouza is Kirk Allison, who's the

director of the program in human rights and health at the University of Minnesota School of Public Health and a member of the graduate faculty of the division of health policy and management.

Then next to Kirk is Dan Cherkin, who is a senior scientific investigator with the Group Health Research Institute in Seattle and director of the Bastyr University Research Institute.

Next to Dan is Liz Jacobs, who is an associate professor of medicine and population health services, vice-chair for health services research in the Department of Medicine at the University of Wisconsin School of Medicine. There's a subtle but real Midwest flavor here, you probably picked up on that.

Next to Liz is Lisa Hopp, who is the director, yes, the Indiana EPC, who will share with us her experience and then next to Lisa is Ting Pun, who is a full time caregiver and a student of multiple sclerosis and neural imaging for the last several years with a strong background in a variety of things from nuclear physics to health IT.

So, why don't I turn things over to our panel?

MS. YUSUF: Thank you. So, to self-identify myself, in addition to my professional background that Paul mentioned, I'm the mother and caregiver of a child with sickle cell disease -- can you hear me? A little soft? Louder? Okay, let me get closer to this.

So, I'm a parent to a child with sickle cell disease. So, I put on that list that I was a patient and a patient advocate and a caregiver, so many hats, as Rachael mentioned this morning.

So, I'm going to actually talk about two items -- two perspectives of my experience with the process that we carried out, one was the composition and the selection of the group that did the process, and the other one is the software tools that we used.

So, if you looked at the bios that were in the registration packet, you saw there was some diversity in the groups that carried out this process, in terms of professional and personal

experiences, in terms of background, in terms of expertise in science and research.

But what most of us -- how most of us came here is we know about PCORI, we know what they do, we went to their website, we applied, and that's how we ended up here. But what about people who don't know PCORI? So, did they get selected out of the process? How do they get involved in this process? And is there some diversity lost as a result of that?

So, some of the things I'm going to mention have been talked about earlier today and one of them is trying to do a more intense recruitment process to try and get people who would not normally be interested in what PCORI does or who don't know about PCORI, so some sort of a pipeline for recruitment using the media, social and traditional media, using advocacy groups, people like us who are here today.

So, I recently told my hairdresser to go to the PCORI website and submit a question. She didn't know who PCORI was so I told her a little

bit more about it. I also thought we could invite elected officials and hospital administrators, people who will be making decisions when it comes time to implement the results of this process, the results of the studies that are carried out.

So, the group selection, I don't quite know how some of us ended up -- I heard there were 160 applicants and 35 of us were chosen, so I don't know what process, I'm sure some sort of a systematic selection process occurred, but I would suggest that the groups not be static, a little bit more dynamic, so depending on the topics that will be researched or that will be privatized, to change the composition of the groups to reflect that.

And one other point, Liz and I met last week and she -- we were talking about how it would be nice to pair up those of us who are part of the process, pair up somebody with some science background, with somebody who doesn't have a science background, and conversely pair up somebody with a disease background with someone who doesn't have that disease background.

So, we used -- my group used two software tools, Survey Gizmo and Expert Choice, and Rachael mentioned them this morning.

I'll just give you the pros and cons of each and how I went around making things a little bit easier for myself. I found the Survey Gizmo to be simpler to use, it took less time, and it gave me some sense of head-to-head comparisons of the topic.

The disadvantages were, I found that it had some subjectivity and I don't like subjectivity that much. And with eight criteria and ten topics, it was a little bit challenging to apply -- to figure out how to give the points to each topic.

So, what I found helpful for myself was to create a table where I put in some of the most important information from the topic briefs for each criteria and then I had something visual that I could use in assigning my points.

For the Expert Choice, we were ranking each -- we were basically looking at each question and seeing how well it matched the eight different

criteria, so it was objective. It was easier to use, I found it easier to use anyway, but it was kind of long. There were 80 decisions that we had to make.

The scale was long, it was an 11 item scale. Some of the wording was a little bit ambiguous, so it made it hard to distinguish between certain levels of the scale, and if found that it lacked some head-to-head comparisons of the topics, and I'll come back to that point in just a second.

So, my recommendation for that is instead of taking a topic and rating it on how well it met the criteria, how about we take a criterion and then see how each topic ranks within that criterion, so that way we'd have some sort head-to-head comparison of each topic based on the criteria.

And you saw the results this morning, the group that I was in we used the two tools and the top two ranked topics and the bottom one were the same whether you used Survey Gizmo or whether you

used Expert Choice, so I would say some sort of validation occurred at least among the top and the bottom. So, could we keep using that because we don't know whether a different group who would use these tools would find the same results.

And one final point is I would be very happy to see everybody that I talked to on the phone and were on the conference call. It would be nice to have future panels meet face-to-face for some part of the process.

Thank you.

DR. WALLACE: Thank you.

[Applause.]

MR. ALLISON: Thank you very much. I'm Kirk Allison and I have a number of interest areas, one is equity in research, health disparities, and disability research, and I also do, myself, some empirical outcomes research as well as social context research related to health and human rights in these various areas.

I think I'll read through my remarks so I can stay within the time.

There are two PCORI prioritization levels, as we know. One is the prioritization of the topics, which is what we're doing now. The second is a prioritization of the answers to the calls for projects. And I think in both of these, one suggestion that I would have would be to intentionally include non-physician practitioners and explicitly named, such as eligible and funding calls, and include them as evaluators depending on context.

For example, one area that I'm pretty familiar with is disability contacts with occupational therapists. Occupational therapists do not have a high prestige ranking in medical circles. When one thinks of clinicians, one does not immediately think of an occupational therapist, for example, but they have rich exposure to the lived experience of people with various impairments with a problem-solving skill set at the frontier of the person and the environment.

In other contexts, midwives, nurse practitioners, physicians' assistants, pharmacists,

et cetera, have important practice-based insights both for prioritization panels and for evaluating research proposals.

In funding calls, those not explicitly named, although theoretically eligible, are often not considered because PCORI is very much an in-house operation. There can be sort of an ethical, value-based leaning against that tendency, but when one's thinking of clinicians, how often does one think of, okay, the PI would be an occupational therapist and the co-investigator would be, perhaps, the physicians if it's dealing on more of an environmental nexus.

Non-physicians may also highlight new topics for prioritization as to patients. For example, I had a recent conversation with a colleague who is an occupational therapy professor and I won't give too much more information, but he remarked that cancer-related disability and mitigation is under research even as cancer is increasingly becoming, in many areas, a chronic disease.

There is a lot of cure focus, but as the curative aspect moves forward, it becomes more chronic, then there's a lot of downstream disability-related issues, both in terms of long-term treatment plans and other dimensions that don't get as much research attention, and he articulated this as being a kind of bias of cure over mitigation, for example, or amelioration, and I think we have to have both dimensions and sort of see the dynamic disease profile as a piece of this.

Some others have other comments to add to this. I know Ting Pun has some good comments and I won't steal his thunder on that.

The PCORI process is different in focus than my last prioritization process exercise that was on evidentiary standards for comparative-effectiveness research with regard for disability. In that context, there was much attention on evidential hierarchies rather abstractly at the beginning, beginning with randomized control trials and then sort of everything else was seen as deficient in comparison.

But as the conversation went on, it ended much more context-sensitively concerning evidentiary strengths for specific contexts, and particularly, for example, in disability where there's a lot of idiosyncratic dimensions, case studies can become very, very important, for example. Or if you're thinking about process downstream, the question of, how does a treatment or an intervention become functionally effective and sustainable, then process issues of downstream practitioners, for example, a lot of -- a number of occupational therapists have said to me, this would be really great, I wish I could do this for my clients, but I can't be reimbursed for it, and if I can't smuggle it into a category that I can get legitimately reimbursed for it, I feel like I'm doing fraud. So, that's a dimension.

Now, I should move to my comments on Expert Choice and I'll leave Survey Gizmo, which was the global scoring tool, to the slide for the moment.

PCORI has found that the eight criterion

may be too many and proposed dropping one patient-ordered criterion, which is inclusiveness, and perhaps seeing that as more appropriate at the proposal level, and a system-oriented one, health system performance. Basically, theoretically, what's not differentiating at the level of the topic, it's best to drop it, that will actually increase the discrimination across topics.

The Expert Choice's summary boxes were somewhat hard to read, but helpful. The nine scoring levels, as mentioned before, were too many and probably too high, too mid, and too low, paying attention to Miller's magic number, you know, seven plus or minus two, nine is kind of at the outer side of that. Probably six is good.

I found the graphical representations quite helpful and that may even be more helpful for non-specialists.

The analogue ordering of scores for the topics made the strengths and weaknesses within each more easy to grasp, and also, alternative graphical scales in the show results, there was a

drop down menu, and it provided a priority view, which some -- each, partially to 100 percent, a little bit like Survey Gizmo.

There was a percentage of the maximum, which normalized the highest as 100 percent and adjusted down. There was also a multiple of minimum, which set the lowest at 100 percent and scaled up, and it made it reading a little bit like an odds ratio and I think that would be -- those sorts of graphical representations would be very helpful and intuitive for people who aren't statisticians, who are not professional practitioners and researchers, and there's also an un-normalized representation, which has provided aggregate averages across all the criteria.

I agree with Fouza that providing, perhaps, a graph or a matrix, which includes comparative scoring across all the criteria at the end for sort of an overview at the end might be helpful and then you could sort of have a global judgment sensibility, perhaps, to adjust some of that.

Again, the instrument -- oh, one thing that I would add, there was a question after using the survey tool, did you use outside information, and I think that should be integrated into the Expert Choice survey tool and use, for example, for speed and efficiency, radio buttons, which could say, what kind of information did you use? Did you use it from clinical studies that you know about, from your patient experience, from your own personal experience, from family experience, and maybe have a comment box for other, and that would provide information both in terms of what is informing the particular judgment, but also other forms of information and sort of other avenues that could perhaps be also integrated into the case descriptions and in even garnering, perhaps, new areas that need further attention.

It's clear that a person could be a physician, but just because one is a physician, it could be a family experience, it could be their own personal experience, it could be the clinical context. In all, I found Expert Choice to be a

more useful tool than the global Survey Gizmo, but I know Dan Cherkin has some positive things to say about Survey Gizmo and so I will pass that on to him.

[Applause.]

DR. WALLACE: Thank you.

MR. CHERKIN: Well, it's a real pleasure to be here at this -- one of many important events that is going on with the birth and the childhood -- infancy of PCORI and the people that have been assembled here on the stage and that were on the phone and in the process of our work on the taskforce was really inspirational to see the kind of people that are attracted to this important mission.

My perspective is that mostly of a researcher who has spent 20 plus years doing research evaluating treatments for back pain, and these have been mostly pragmatic trials and, I believe, patient-centered, although PCORI is raising the bar on what we can call patient-centered.

So, the main focus of my comments are focusing on the issue of the prioritization criteria and this has been a moving target, because when we first talked about them, there were eight, now there's five, so I was editing my notes as the morning went on.

But I think really -- so, the real question, I think, is how to optimize the relevance, clarity, and parsimony of the criteria, at least that's my view, but I think there's an overriding issue that relates to a lot of the topics here that I'll use in illustrations as we go ahead, and that is, there's a distinct and important distinction that has been a bit blurred in many aspects of PCORI-dom between the criteria used to evaluate research priority topics, and to select the highest priority topics, versus the criteria used to evaluate grant proposals submitted.

And there's been just a number of situations where I've been kind of a little baffled because there seemed to be a confusion between

those two.

So, the current view from PCORI is that patient-centeredness is an essential component of the criteria, that if it's not patient-centered enough, and I don't know how they'll evaluate that exactly, specifically, but then it doesn't go forward. Fine.

Impact of the condition on individual populations, fine. Differences in benefits and harms reduction and uncertainty have now been combined. Implementation and practice or the potential for improving current practice, I think, is really what that gets at, and then durability of information.

And so, I think these changes really are valuable and help simplify the process of evaluating topics, reducing overlap between the criteria, and increasing the focus on the most important criteria.

But I have a couple of comments. First, I think making patient-centeredness an essential threshold criterion is fine, but it's a complex and

multi-faceted concept that those ranking priorities need to understand, and I think some of the instructions that we were given were a little bit confusing.

The descriptions of the criteria for patient-centeredness should be modified when applied to ranking research priorities as opposed to evaluating specific research proposals. For example, the question, "does it focus on potential outcomes that are most important to affected patients?" does not really make sense when you're talking -- trying to rate or rank research priorities. It's something that's going to be determined by what the grant applicants suggest to use as an outcome measure for a specific study.

The other issue is, I'm really not sure about the value of retaining the durability of information criterion. I found it very difficult to assess, and people that aren't really -- don't have expertise in a particular area, are really having -- going to have no idea, and even some that do have expertise are probably going to have

trouble, and some of the topics we evaluate specified the treatments to be studied, for example, percutaneous coronary interventions with bare metal stent, drug eluding stents in coronary artery bypass grafts for a coronary artery disease, while others left the choice of treatments to be compared to the grant applicants, comparative effectiveness of management strategies for back pain, for example.

So, the specification of the treatments to be studied needlessly, I think, precludes opportunities for evaluations of less traditional but possibly more innovative approaches. For example, many patients rely on complementary and alternative therapies for conditions such as muscular-skeletal pain, stress, fatigue, irritable bowel syndrome and many others, and I think it would be very un-patient-centered-like to restrict research on important topics to only more traditional or conventional therapies.

So, if the topics were less prescriptive of treatments, then I think the durability of

information criterion is really only relevant in the evaluation of specific research proposals submitted to address those top priority topics, which is a task for another group.

So, one final comment on the software tools, since Kirk mentioned that you could look forward to this from me. I think there are clearly tradeoffs between the Expert Choice and the Survey Gizmo and I understand that many, maybe most, who used both preferred the Expert rating choice, but I think if the ultimate goal is to identify the highest priority research topics, then it would seem that we'd want to approach that directly by comparing the different topics with each other and how they stack up, one relative to the other.

Now, yes, is there subjectivity? Absolutely. But is there subjectivity in all of this? Absolutely. In some cases, we can come up with more quantitative, ostensibly more objective measures, but I'm not sure, really, that it really ends up being more objective.

So, I'd argue that a ranking system like

the Survey Gizmo approach accomplishes this better, that is, of the relative value that is going to be using implicit weighting, at least, of individuals, but I'm not sure that's all bad. It may be more difficult, but I think it may be more valid in some ways, and at least maybe it could be used once at the last stage where there's a simpler process for narrowing down the thousands, millions, or whatever, to a smaller number, 10, 20, whatever, and then doing this.

So, that's it. Thank you.

[Applause.]

DR. JACOBS: I wanted to start by talking about the perspective that I came to this with and to make a sort of broader plea for how we can actually engage people at many different levels of perspective.

So, we were asked to choose what was our main perspective and my main perspective is a researcher, that's predominantly what I do, but I'm also a disparities researcher, so I really come at it from an angle of disparities and often the

populations that I'm interested in reducing disparities for are really underrepresented and maybe underrepresented in some of that evidence that was shown today.

So, I also come to this with the perspective of, are we including the voices and the populations that we really need, but I'm also a general internist who practices in a federally qualified health center and before that practiced for 12 years at Cook County Hospital, so really in safety net institutions. So, I also come to this with the safety net perspective as well.

And then I also was the primary caretaker for someone who was severely ill for two years, and so I also bring that perspective. And there's many examples, Fouza is one of them, I know I was talking to Linda Morgan last night, people who come to this, they might say they're a patient or caretaker perspective, but they come with also the scientific background and that I think that one of the things that PCORI might want to do is, first of all, really trigger people, instead of saying, come

at this from a researcher perspective, which is -- first of all it's very hard for you to take out those other biases or other ways in which you think or look at the world, but ask people to bring in that diversity of thought when they're actually looking at this prioritization and trigger people to actually use all those perspectives instead of just as a researcher, just as a patient advocate, just as a clinician, I think is really valuable.

I have to say, I couldn't come at this and do this process without all those perspectives. And that it's good to actually -- when you think about asking people to nominate themselves and say who they are, to choose as many as they want and say why they think they fit in all those categories.

I think having someone who really understands the patient side or provider side in addition to the scientific side is actually really, is really key and would really help you in your processes, so that's one of the points that I wanted to make.

I also wanted to talk about the research briefs, which I actually found quite accessible because I think about research all the time and as a primary care doctor, I also look at summary of evidence a lot to help guide my own practice with my physicians -- maybe I'm the only primary care doctor that does that, if you look at the research, but I do try to go from evidence, and so I'm really familiar with that method of evaluating evidence and strength of evidence and what's missing and what's not there, but there are a lot of people on our panel who said either, one, that it was not enough detailed information.

And I don't know, many of you in the room probably don't have access to those briefs to know kind of what detail they're at, but they were somewhere in between -- and then there were other people on the panel who said, this is not accessible to stakeholders, like if you're going to get someone from the community, let's say a community I serve on the south side of Madison who may not be highly literate but really has -- is an

advocate and has an important voice and perspective but can't really get the depth of the scientific information, what do you do.

And so my recommendation is that you have sort of an executive summary that's really accessible and then there's more depth to the extensive brief. If people want to go to that, they can. They don't have to.

And then the last thing that I wanted to comment on is we were asked on the panel if we really felt PCORI was having an effect on making people think about the patient-centeredness of research.

First of all, I found it very rewarding in both our panels that when we -- there was also something we did where we actually ranked the importance of the different criteria, the eight criteria we were given, and patient-centeredness, by far and away, came about ahead as the most important thing that we used in our evaluation of these research briefs, and I found that very rewarding that people are now thinking from the

patient-centered perspective and I can tell you that -- but unfortunately on the research side, you know, there is really this cultural shift and cultural change that has to take place.

I think about it a lot because I'm a disparities researcher and a lot of time I'm getting people who don't naturally think about people who are different from them, to think about what are some of the problems they face, how do we overcome those problems, how do we address them in healthcare, but a lot of physicians and researchers don't think that way and I've had people come to me and say, I'm going to submit this application, will you look at it and tell me if it's patient-centered, and I can tell you they're not very patient-centered.

And so I really think, you know, for instance, people were really looking at how a hospital was going to save money and that is an important question, but it's not necessarily patient-centered, because that might help the patient if that hospital then takes that additional

revenue and goes out and does something in the community, but most likely not, it's not necessarily a question that might be patient-centered.

So, thinking about how we can expand that, I think that these kinds of opportunities and kind of inculcating, culturating some of us into the PCORI process that we can go out and disseminate it I think is really important.

[Applause.]

MS. HOPP: Hi there. I'm going to try not to be too redundant from what Liz has said, but a lot of what I'm thinking about is very similar to what she said.

My perspective is primarily from the researcher point of view. I do run the Indiana Center for Evidence-Based Nursing Practice. It's EPC AHRQ funded EPC, but rather part of an international collaboration of about 60 groups and centers around the world interested in all aspects of evidence-based practice in healthcare.

So, the patient-centeredness was really

what was keenly interesting to me, like everyone else. I think from my discipline perspective of nursing, we have claimed that that's at the core of our being, but I don't think that we have the corner on that market for sure.

So, I was just going to make two, sort of, major points. In order, I think, for patients to be engaged in the prioritization endeavor, they need to be prepared for that activity, and while they're -- by the counts, there seem to be good equity and balance amongst the groups represented, it didn't feel that way.

So, even when prepared -- my second point is, even when prepared, the methods of communication and process must allow for authentic collaboration and we've heard a lot about the need for simplification of the topic briefs and the processes, as my partner in crime in this process, Suzie, said, it has to be short enough for her Google brain.

So, I think some of the themes that we discovered during the prioritization process have

already been identified in the workshop that PCORI held in October about identifying/selecting the research questions, and PCORI's taken some excellent steps towards shifting the paradigm toward patient-centeredness, but still the topics and the descriptions for rating still seem quite provider- and research-centric to me, and written for researchers rather than in plain language.

But even if those topic descriptions were written in plain language, I think that patient-participants and even others will need better preparation beyond the guidelines.

In October, participants said speak clearly, demystify, educate, train for the role, and they need down and dirty guides to how to read these proposals or the prioritization topic briefs. I think that there were hints to us along the way, questions that told us a little bit more about what that criteria was about, but I think that there needs -- those hints need to be there about what questions do you ask to know if this was a prioritization.

I wondered if one of the things that might help us with the patient-centeredness criteria was to look at evidence from qualitative research about the meaning of the patient experience. We haven't talked about that here. We're very centered on comparative-effectiveness and obviously qualitative methods are not appropriate to determine effect. However, we conduct systematic reviews of qualitative research about the meaning of experiences from whomever the point of view is, and I think that could inform some of that patient-centeredness.

So, if we understood better, for example, what the pain experience is in chronic back problems, that might help inform that patient-centeredness.

I just wanted to talk about a gentleman who had a big impact on me when I attended a knowledge translation conference in '08 in Banff. His name is Michael Gibbons. He's actually an engineer and he's an author of a couple books including *Rethinking Science* where he proposes a

shift from mode one, or curiosity, researcher-centric, investigator-derived types of science where you have end of grant dissemination and, with any stroke of luck at all, implementation of that evidence.

He talks about mode two research, which is about knowledge exchange that is generated within the context of application so that knowledge users are part of the society, are drawn into the engagement process throughout the knowledge generation and exchange, just what PCORI is about from my read.

He argues that boundary objects are necessary for this knowledge exchange to happen. These boundary objects are the way that experts, knowledge users, any stakeholders, finds a way to effectively transform an issue or problem for research and he uses a simple metaphor that helps us understand what these boundary objects are. He talks about a man and a woman who are strangers and they're walking in a park, and they want to find a way to talk to each other, but it would be a little

bit socially awkward in order for either to approach the other because they wouldn't know the aim of the conversations, what the intentions are, that sort of thing, and they're just too ambiguous and they may even be defensive at first.

So, however, if they are both walking their dogs, the conversation may begin around dogs while other issues are in the background. So, the dog is the boundary object. And he argues, and I wholeheartedly agree, that we need to find the right dogs and the way to talk about them in order for legitimate, authentic patient engagement in the entire process of the research endeavor to occur.

[Applause.]

MR. PUN: First, I want to thank PCORI to give me an opportunity to actually get involved in this prioritization process and also involved in the patient-engagement workshop. Okay. I'd like to also thank Rachael, Katie, Natalie, all the people that are involved in that, that make this whole process very, very enjoyable.

So, being the last one to talk has a

certain disadvantage. I want to make sure I have something to say, so I have two -- I have only one and a half point to make. But before that, let me make sure to respond to Kirk's mention of my name. Actually, it's because during a conference call I make an off-handed remark that the best candidate for prioritization, physician/clinician -- no, I shouldn't say that -- physician/researcher, okay, but also have a chronic illness. So, those would really have the knowledge, they also have the experience, and really help out in doing this prioritization.

Okay. So, the half point I want to make, because right now it's been pretty much common agreement that the frontline physicians, frontline people doing the healthcare, should be involved. So, the only half comment I have on that is what about PCORI actually coming up with some mid-career fellowship for frontline healthcare providers to get involved in PCORI-type of research.

So, I'll go to the other point I want to make, which may be a little bit marginal, okay, I

was thinking about what to talk about and I happened to be involved as a patient advisor in Palo Alto Medical Foundation, and last year I actually help a little bit in sort of reviewing, screening the applicants.

There are two questions in there, I want to read it exactly, they asked the potential candidate. One is, list three characteristics you consider important in good patient care and service. The other question is actually, describe some of the things you think healthcare professionals could do differently or better help patients and their families. So, I thought it's pretty much patient-centric.

SO, I look back at all the applications, okay, well, to get into statistics, okay, there's about 11 or 12 of them, ranges from age of 20 to 70, from young mothers to actually cancer survivors also. Okay. But the three top answers that really stands out, one is, listen to the patients. Two is improve, detect, doctor/patient communication. And the third one is compassion. Treat the patient as

people and learn about them.

Okay, so I start staring at it while 49ers are losing to the Rams, and what happened is it just dawned on me, all these questions are really the care part in healthcare. It's not so much of the health, but really the care part. And since I have no idea of how to do research or do anything exposure to sort of a so-so science type research, okay, so I raised some questions about how do you do CER for these type of questions, and I was curious if Rachael from the collection of questions, was any type of -- this type of question being brought up.

So, how do you do it? I really don't know. So, anyway, so the last thing I want to say is, from my short encounter with PCORI, I met a lot of people, well-established people, and they are very open-minded, maybe that's a bias already, but based on that, I really feel that PCORI would be very successful organization going forward. Thank you.

[Applause.]

DR. WALLACE: Again, to further sample really the alpha testing experience of our explorers here, but maybe I wanted to kick things off with maybe just a couple of comments and a couple of questions.

So, I'm like an old quality improvement guy and we've had a lot of models flying around today, but I think when I sort of feel sort of model-fatigue, I tend to retreat to the models that I'm most familiar with and I think the old Donna Beatty-ian context, in the spirit of quality improvement isn't a bad one, to think about structure and process and then aiming towards desired outcomes.

And I think it struck me that each one of you started out talking about aspects of the structure of the process -- of what you went through and then also some specific comments about process.

But there were a couple of things that particularly struck me in thinking, perhaps, at the structural level where -- and I think we've seen

this modeled today, where historically, if you think about how we've created study groups, we've tended to engineer out heterogeneity and we've selected strongly for single types of expertise or areas of focus, and what strikes me in an almost through the looking glass manner about what's occurring around the discussions around PCORI is the pursuit of people who have multiple perspectives.

So, I think we've talked about diversity in terms of the inter-personal diversity in a group, but there's this other dimension of intra-personal diversity of the experience that strikes me as has actually been modeled in a variety of ways, both today and by the panel.

But I'm wondering if -- what your reaction is to that? Is that an important part? Is that something you would see that should be encouraged as opposed to, perhaps, some other settings that we engineer that out? And what are the opportunities for really bringing that out, from your experience?

MS. HOPP: Okay. I actually was struck

because when listening to your perspective and how valuable it is to have multiple perspectives, we're all consumers, we've probably all cared for a loved one in some way, and we've all been sort of hit in the face with being on the other side of the coin. We talked about that.

But, it seemed to me, during this process, we were defaulting to the position of strength, which was as researcher-clinician, et cetera, and it was really easy to forget about being the patient or the caregiver in this process.

So, I think it is valuable, but I also think we need some folks involved in this that are sort of purely bringing that perspective. And I don't know if it has something to do with power structures or whatever, I'm not that kind of researcher or thinker, but it felt that way. It was weird, because I know we all have those other experiences, but we had to concentrate on those, on bringing that forward.

DR. WALLACE: Liz.

DR. JACOBS: To add to that, I think part

of it is the way in which the process occurred, which is a very highly scientifically structured process sort of like -- so, it cues you, I mean, in all sorts of social situations or situations you're cued by what's going on around you to what you're supposed to focus on, and so I think it -- that's why I was thinking it would be great to cue people to think more broadly. I mean, even starting some of these research briefs with a vignette, a patient vignette, would be a way to get people in the mindset or perspective of the caregiver to give people a mindset of, oh, we're thinking of more broadly than this evidence here.

DR. WALLACE: Dan.

MR. CHERKIN: I think one of the key distinctions between what PCORI is trying to do and, say, NIH is, that PCORI is explicitly patient-centered, and that's as opposed to disease- or clinician-centered, and so I think people that would be attracted to PCORI are going to be more homogenous in the sense that they value the perspective and experience of the patient.

And so, in a way, that's homogeneous, but it is also the organizing principle of this whole organization, and I think, really, the important thing is that beyond being able to look at the patient perspective, there's the skills and insights that can look across the experience of the clinical healthcare systems, et cetera.

And so, I think most of the people here, I believe, that have been attracted to PCORI, really have -- are very diverse in that sense, and the intra-diversity, I guess, I think is important, but the unique thing of this group and the organizing principle, I think, is the patient-centeredness, which has been largely neglected by previous government funding.

DR. WALLACE: Yes.

MR. ALLISON: I was thinking also that a lot of the problems in the descriptions or in the case briefs, they were very much clinical intervention on a specific physical malady sorts of orientations, but PCORI has five areas, sort of, domains that they're indicating their interest in

from health disparities to information dissemination to systems approaches, and I think what the patient-centeredness means in those different domains sort of shifts and moves. And then also I think who is the occupational therapist in the informational dissemination domain, in a sense, is going to change.

And I think thinking systematically about who are those people that are at the interface between the patient and the information or at the interface between trying to figure out what are the central determinants of health disparities that are related to socioeconomic status, it could be things as easy as clinic hours, availability, transportation, and some of these mediators that get in the way of having effective treatments actually implemented or making them sustainable in patients' lives, I think, thinking broadly in terms of those and sort of -- and analyzing who's on the margin that can be brought into the center.

My sister is a nurse. She was a cardiac unit intensive care nurse, then an ER nurse, and I

remember this story which she said, I marched down to the medical director's office and said, you have to get a hold of these residents because some of them are going to kill my patients because one's coming in and doing one thing, the other's coming in and doing another thing, but she had the 12 hours on the floor observing how changes in protocols and how treatment directions were being applied quite differently and sometimes contradictively.

But she was the point of information for that, for the medical director, and so I think the question is, on the front line, who are the people that pulled this more proximate information and how was this also brought in to identify areas of, say, process research or quality research and these things.

DR. WALLACE: Let me just ask one other question -- maybe we could ask Fouza and Ting first, you know, when we started to take this metaphor of thinking about structure and then process, one of the transitions is the brief. It's

actually how we positioned to actually get people engaged in the process, but it's probably the trickiest piece of this whole puzzle. I mean, I think a lot of us kind of fought hard when we recognized how much that hinges on.

So, I think a lot of the tension here is sort of, to what extent was what you saw helpful and do you have a particular suggestion for things that would be really critical for incorporating into the beta version and thinking particularly about the briefs? So, maybe we'll start with Fouza.

MS. YUSUF: So, the briefs were helpful, but some topics were covered well and others were not, so there was some imbalance, there were some inconsistencies, so I think if they are made more consistent and if the information is more comparable it might make it easier to use.

DR. WALLACE: Okay, so consistency is clearly going to be a piece, and Ting, other --

MR. PUN: I actually question myself while doing the whole prioritization because I have

exposure to rare disease, caregiver, so I ask myself if actually there's a one topic about rare disease. Would it bias my judgment? How to keep to be objective, okay, to be able to do the prioritization?

So, that -- the sort of emotion bias could have some effect and I don't know how to correct for it, for example.

DR. WALLACE: So, there's a range of biases that we'll have to be sensitized to and probably because of the complexity of the process, there's biases that we haven't really thought through.

Other thoughts from the panel about -- yeah, Dan.

MR. CHERKIN: I think I'd worry more about the people who believe they have no biases than about the people who are aware of them.

DR. WALLACE: So, beware of the bias-free person. Anyone who thinks they have no conflicts of interest, perhaps has no interest.

[Laughter.]

DR. WALLACE: Any -- yes.

MS. HOPP: I think, you know, I was sort of crying out for some more plain language with it. There were the lay summaries, but they still were fairly high level.

I think more graphical presentation of information may be helpful, so using infographics if that's possible. I'm just really glad that I wasn't the one having to write these briefs because, as Rachael said, it must have been a terribly humbling experience. So, I think we all appreciate how difficult it must be.

But any way to simplify yet keep the information and meaningfulness within the topic, I think, would be more than helpful.

DR. WALLACE: And I think it brings out the theme that came out earlier that simplify doesn't mean simplistic.

MS. HOPP: That's right.

DR. WALLACE: It actually is probably more elegant. So, I think that's a high bar.

MR. ALLISON: And perhaps just as an

editing process, to have some outside lay readers that you draft from the community or somewhere to read these would be helpful.

DR. WALLACE: Great. Well, let me open it up and see -- these are your alpha testers. If you'd like to know what this is like in the real world, this is your opportunity. So, please, let me see who has questions. I think we have a question right here in front. And again, I'd ask you just to identify yourself and your organization.

MS. KENT: Hi. I'm Erin Kent. I'm with the Outcomes Research Branch at the National Cancer Institute and I just wanted to say that all of your comments I really resonated with. I was a participant on the pilot prioritization process as well.

I really wanted to just come back to a point about how PCORI has this unique opportunity to be very patient-centered as opposed to some of the, you know, longstanding agencies like AHRQ, like NIH, that have been doing outcomes research

for a very long time. I want to just mention that I think it's going to be very important moving forward for PCORI to continue to have conversations and dialogues with those agencies so that they can both learn from some of the best practices that those agencies have used over time, but also teach those agencies about the best practices that they develop.

You know, and I also think some of that conversation can be at the level of advising investigators who are committed to doing patient-centered research where they should best apply and how they should best structure their proposals and their research ideas to be patient-centered. I think that it's an opportunity for those agencies to become more patient-centered and I think that, you know, that sort of partnership moving forward can be very helpful.

I also wanted to comment, I really, really like this idea of boundary objects and bringing that onto the table for the prioritization, for the review processes and it came up to me when I

thought about how, you know, in grant -- of these study sections and those study sections can really make -- they do impact or have an impact on scores that reviewers give to grant proposals as they come in. You see shifts where reviewers come in with a certain score and then after the conversation, after the discussion, their scores shift.

And so I wondered if we had had, you know, more in depth discussions as we were reviewing the topic areas, how our scores would have shifted, but that that, in this more patient-centered setting where we have stakeholders who wear multiple hats, come from diverse backgrounds, how we really then -- it's so much more important to acknowledge those sort of, you know, subconscious power structures and to bring things like boundary objects, maybe in the form of vignettes or something so that we're all on the same page and people feel comfortable voicing their interpretations and their opinions about the ways that they're evaluating research.

So, I guess those were more comments than questions, but thank you.

DR. WALLACE: Thanks. Let's see, over here.

MR. BASU: So, this is Anirban Basu from University of Washington, Seattle. My comment is actually following up Dan's comment about simplifying some of these criteria for prioritization. And when I think about prioritizing large topics, I wonder the value of putting patient-centeredness and also reduction of uncertainty in there, because if you think about a topic like radiation therapy in prostate cancer, you know, you don't quite know what level of patient-centeredness you would get from specific applications. Right?

So, at that point you're only trying to kind of see if it has a large impact on patients' health and whether further research is worth doing.

Similarly, reduction of uncertainty, I mean, that's a topic that's really study-specific, and maybe some of these criterion could be actually simplified and to just give the impact on population health and to at least prioritize the

topics to begin with.

DR. WALLACE: Dan?

MR. CHERKIN: I totally agree that the -- I made a comment that I think the concept of patient-centeredness is very tough, and in the example you give, it's not obvious where is the patient-centeredness necessarily, and patients -- most patients have no idea of what is going on behind the curtain. But were they to know, they might have some new ideas about what would really matter for them.

But those of us who do know what's going on behind the curtain may understand that some of those things that are going on really are not in patients' interests, and were they to be more evaluated explicitly, could greatly benefit patients.

So, I think while patient-centeredness is critically important and a hallmark of PCORI, we have to be very broad in how we kind of look at that.

The other thing is, I think that in -- I'm

not sure I agree that we can't, the issue of uncertainty, I think, can apply to topics. That is, if there's a clinical conundrum, what's the best way to do things? That is the uncertainty. I mean, it's not -- the answer to it could be any -- depends on what the -- if that's a research priority and applications are invited, then each of the proposals may be looking at a different aspect of it with different degrees of impact on uncertainty.

But I think the global topic where we really don't know what the right answer, that's inherently laden with a lot of uncertainty.

So, I don't know if that missed your point.

PARTICIPANT: [Off microphone] -- as long as we know the specific study.

MR. CHERKIN: Fair enough.

DR. WALLACE: Okay, in the back, and then we're going to come up here.

PARTICIPANT: I just wanted to sort of respond to Ting's comment about his thought that he

was being biased as a caregiver or someone with multiple sclerosis. I'd just like to respectfully suggest that you're not at all, and that we shouldn't be thinking -- I think one of the reasons you were chosen is because you are a caregiver for someone with a disease, and if there was a -- I mean, if there was a clear truth that we're after here, then maybe we should be talking about bias, but if there was a clear truth, we wouldn't need people looking at these scenarios, we'd just have some computer, you know, do an algorithm and come up with it.

So, I mean, I think your thought about thinking, gosh, I want to be fair about how I characterize these scenarios because I do come from this background I think is absolutely fantastic, and we do want open-minded people on these panels, but I really do think we shouldn't be talking about, you know, individual experiences as biased because you're being chosen because you do have those experiences, at least that's my view.

MR. PUN: Actually, from the result of

these two groups, you know, the results are pretty much similar. I have a lot of confidence, actually, pool a group of people by various background and so on, you still get a very consistent result. That has actually given me a lot of hope for that.

DR. WALLACE: So, we have up here.

DR. WEISMAN: Just commenting on whether patient-centeredness should be a formal criterion. I'm just observing this workshop, the one yesterday, and other ones in the past and hearing what participants say. It seems to resonate and really affect those who are talking about it as being something important, but it also creates a, I think a discomfort, as scientists about what do you do with that because, you know, we are comfortable and less vulnerable as individuals when we're dealing with objective information and we tend to objectify and take the humanity out of that object called a patient that we're treating often.

And it is this clash, almost, but I heard, Kirk, when you said that we were asking about the

physical maladies and the interventions that could be applied to them. That's a comfortable thing for PCORI to be talking about, it makes us sounds scientific and we can talk about patients'' perspective, but it keeps us totally in the physical plain of treatment and care, yet each of you has talked in various ways of things that extend beyond the physical manifestations of disease to the complexity that goes on when you're dealing with it as a human being to human being.

You know, Liz, you talked about disparities and dealing with people who are in minorities who don't speak the same language and how do you communicate and how do you -- and there are many things affecting aspects of their health and their disease treatment that goes beyond the objective measurement of lab findings, bio markers, physical findings, X-rays, et cetera, but that tends to be the realm of research where we feel comfortable.

And I'm wondering, as a panel, since I picked up from you, you all were touched by this

notion of patient-centeredness, how do we take what is many times perceived as a non-objective, non-scientific value and put it into research prioritization that is acceptable and is measurable, perhaps, or less measurable, but at least included in what we're doing when we prioritize?

DR. JACOBS: Can I respond?

DR. WALLACE: Sure.

DR. JACOBS: I really think of myself more as a social scientist than one of these scientists you're talking about, and there are certainly objective ways you can measure all these things. For instance, when it comes to language, you can look at whether someone got an interpreter or not and were they a professional interpreter who you knew had the skills to be able to interpret. That's one way to objectively measure were you providing patient-centered care in a language that a patient understood.

I also happen to do a lot of work on the measurement of trust in healthcare and how we can

measure it, and I'm actually really interested in cross-cultural measurement because sometimes we develop measures for people who look like me and they don't apply to other people, and so I'm really -- and you can do that, there are scientific, objective, systematic ways that you can do this.

And so, I think there are definitely objective ways that you can measure these things.

I personally am not comfortable with it because I do it, and I've seen it be done well.

DR. WALLACE: Dan?

MR. CHERKIN: I think the whole reason PCORI exists is because the conventional medical approach to most -- to problems has been fairly narrow and has been largely bio-medical, it has not -- in spite of training the bio-psycho-social model, the systems don't support it in terms of time and training and resources.

So, I think, really, the question is, is there evidence that taking a bio-psycho-social model or more holistic model can be helpful? And I think there is. And I think it's emerging, and I

think neuro science research is increasingly providing evidence for the interconnection between mind and body, and then you get into spirit and that's even more complicated, but -- so, I think this is the frontier, but I think there's plenty of evidence, including if you ask patients, somebody decided that listening and communicating were important, I think we know that, but we don't know what to do with that, and I think by having PCORI here saying that all of this is important, the bio-medical and the psycho-social, we need to not be reductionistic and focusing on any one of those, but rather the question is, how do we help the patient? I think that has to be the organizing force rather than how do we treat the disease.

And much of what people bring to doctors is not disease, it's illness, it's coping difficulties and challenges. So, I think I view this as totally revolutionary at a time that's ripe for this, and I think PCORI is the vehicle that can carry this forward.

DR. WALLACE: That's a great statement.

It's probably also the necessary segue into our next session. I hope you'll join me in thanking our alpha testers.

[Applause.]

DR. JACOBS: Thank you.

DR. WALLACE: We're going to just shift chairs here a little bit. Maybe I could ask the next panel to join us up on stage.

And maybe I'll just give you a little bit of context for what we hope to do in the next hour.

So, in the next hour we're going to try and help Joe and Rachael out because Joe and Rachael have this interesting task, for the last portion after the break, of actually synthesizing all of the information from today and providing us insight and direction about how we're going to go forward.

So, I think that there is an opportunity here for us to think about what are the fine points that we would like to emphasize, what are the things that we would like to create other clarity for, and also, can we share the rich perspective

here in the room to help guide the discussion further?

So, you've had a chance to meet several of the folks that are up here, but let me just briefly introduce the folks who you haven't had a chance to meet yet.

Immediately to my left is David Hickam. David has recently joined PCORI as director of the program on assessment, prevention, diagnosis, and treatment options. He's been an internist for more decades than we care to count, right, and previously has been at the Portland VA and the Oregon Health Sciences University.

Next to David is Michael Lauer, who's well known to folks. Michael is the director of the Division of Cardiovascular Sciences at NHLBI, is a member of the PCORI Methodology Committee, and has a rich past history in health services research and clinical trials at the Cleveland Clinic and has also clearly been a leader in thinking about how we can promote and generalize this discussion around comparative effective research and PCOR.

And then you know Joe. Next to Joe is Arnie Epstein, who's also on the Board of Governors at PCORI, is the John H. Foster Professor and chair at the Department of Health Policy and Management at the Harvard School of Public Health.

You've met Rachael, you've met David.

Perhaps what I would suggest that we could do to kick things off would be to allow the folks who you haven't heard from before to just share with us the elevator speech about what they've heard in this discussion so far. What are your impressions? What are the things that you would begin to help Joe and Rachael out with? What is the synthesis of what we've been hearing? And then, we can open it up a little wider to both the input and the questions from the audience.

David, since you have the fortune of being the closest, so I'm going to ask you to go first.

DR. HICKAM: I think what I've heard, as we've had this conversation throughout the day, is the importance of clarity about the clinical decisions that people make and I should say, we had

a very interesting PCORI conference yesterday in which there was a large number of stakeholders representing all parts of the medical community, and it really resonated that the people are interested in the decisions that people need to make, and then that sort of connects to the essential part of PCORI, which is to focus on patient-centered outcomes.

I thought in the panel that we had just before this one, there was kind of a nice discussion about -- help me here, was it a dog that was in between the -- there was a connection there between the clinical decision and the research projects that might help inform how people can bring better information to those clinical decisions.

And so, it's challenging because when we're talking about prioritizing topics for possible research, we have to sort of loop back around to the decisions that people need to make.

DR. LAUER: About a year ago, I had the pleasure of having a one-on-one meeting with Tony

Fauci. Tony Fauci is the director of the National Institute of Allergy and Infectious Diseases, and was one of the key people who led the research effort on AIDS and HIV, which is a remarkable story.

I remember when I was a resident taking care of people who were my age with newly diagnosed AIDS and they were going to be dead within the year. And thanks to the research that was done, basic translational, comparative effectiveness, clinical trials, the whole mix -- industry, government -- we've made enormous progress, and while this disease is still a big problem, it's been converted from an instantaneously fatal disease to a chronic one.

Anyway, I was meeting with Tony and we were talking about the topic of research prioritization and he looked at me and he said, let me explain something to you. Every single day it is your responsibility to tick somebody off, and if by the end of the day you have not ticked somebody off, you're not doing your job. So, Joe, I'm

telling you that to help you feel good.

[Laughter.]

DR. EPSTEIN: On that note, I was hoping to have a bad day. Arnie Epstein.

This is extemporaneous. I wanted to put something on the table, which hasn't been before. PCORI, thus far, has been a passive receiver of research ideas. We put together expert panels, we're going to grade those ideas, we're going to choose some for funding, and that's all well and good, but now we're going to a much more important stage, either initially or thereafter, we're going to start to identify a relatively small number of areas and ask people to focus on them.

And my thought is that our task is to choose areas in which, when they focus on them, there are lots of opportunities for them to do really important work. Because the alternative is, if we choose areas where there's no opportunity to do really important work, we've really shot ourselves in the foot.

And I was thinking about the value of

information equation, and David, I'd invite you to comment on this later, it strikes me that a key part of that for someone who does investigation, is figuring out what you called the probability in your decision tree that the information you get from research is going to meaningfully change what you choose so that when you multiply out that long but relatively straight forward Benthamite Equation, we improve societal utility.

That strikes me as a challenge that every researcher is really very familiar with. If you think what researchers do, they're trying to put their research in high impact journals. That's really a badge. What they're really trying to do is turn over research that has a large impact on patients' healthcare and health. And one of the ways we measure that is it ends up in a high impact journal.

And that research really starts, all of it, with did you choose a problem that was important, did you choose a problem where there was a lot of morbidity, all the stuff that I think of

on the right hand side, they're all important areas. But what really sets upon good researchers from not good researchers is the ability to identify, I think, when there's been change that lets us have a pocket of opportunity to make advances.

Sometimes those changes are really just exogenous. There are four new drugs in this area and we can test them all. There are six new diagnostic tests, we can test them all, and sometimes it's a matter of just blind ingenuity, but that's actually less common. But you can figure out, are there opportunities there, and I think we need to think carefully -- we're starting to do this with the notion that we're going to have expert advisory panels, and Joe may want to say something about that, but think carefully about how we can identify not the areas that are most important with lots of morbidity and that are going to be durable, because that's the easy part.

I think it's, can we identify the areas where we already have 146 studies, but can three

more make a difference? And for some of those areas, it's yes, and PCORI's job is to pick big picture areas, be it fibroids, be it falls in the elderly, be it cardiovascular diseases where there are lots of opportunities, so if we signal investigators to go searching, they'll find them, versus areas where there's really been no change and not a lot of opportunity.

I'll turn that off.

DR. WALLACE: Great. Well, what we would like to do is have an opportunity for people to pose their questions, share your concerns, share your suggestions. Maybe I'll just take the liberty to build on a theme that I heard a little bit here that, Arnie, you mentioned impact factor and there is a conventionally defined impact factor that I think as researchers we're all quite familiar with, but Michael also mentioned a somewhat different kind of impact, which was actually improving the health of the population.

And in between that is sort of where I think we're trying to go. But I'm curious about --

you know, it also gets to what I mentioned before t hat as we think both about the structure and the process that we want to go through, I would also imagine that to continuously engage patients, we're going to need to feed back to them how their participation in the process has made a difference.

So, what is the way that we're going to close the loop? You know, when we think about an impact factor for this work, what are the attributes of that, and realizing this is still at about 10- or 20,000 feet, but how do we want to think about that? What are the things we're after?

DR. LAUER: Well, these are both important currencies. AIDS is really a great story because the AIDS community was extraordinarily active and played a major role in enabling the research to happen, enabling the trials to happen. And, you know, one way of thinking about this is in order to get high impact trials published in the major journals, you've got to get them done, and in order to get them done, you need to get patients enrolled and you need to get large numbers of patients

enrolled, and in order for that to happen, the patients themselves need to be interested.

And we've seen some neat cases where patients have been engaged, have played a proactive role, and have enabled really terrific studies to get done, these trials then merit getting published in the high impact journals. Because they get published in the high impact journals, people pay attention to them and eventually they translate themselves into practice.

Two interesting areas to think about, one is rare diseases. There have been some rare disease groups that have done fabulous work. There's a very rare disease called LAM lymphangioleiomyomatosis, which is a sort of a pseudo cancer that affects young and middle aged women. There are lesions in the kidney and the lung. It used to be a uniformly fatal disease, it's still a very serious disease, and it's very rare.

But what happened is that the mother of an affected patient, a patient who died of LAM,

decided that she wasn't going to sit around while nothing was being done about this anymore, and so she created a foundation, and this foundation in turn then stimulated researchers at all levels, basic scientists as well as clinical trialists to do something.

And the result of all this was that some important discoveries were made about the biology of the disease and this then led to a trial, and the trial was of a drug called Sirolimus, which has been around for a long time, it's been used for a number of cancer as well as in transplant patients. Anyway, this trial was done and what the trial showed was that one could slow down the progression of this disease and improve quality of life.

The trial involved about two-thirds of all patients with LAM in the United States. The LAM Foundation -- it's because of the LAM patients and the LAM Foundation that this trial happened.

Now, where did the trial get published? It got published in *The New England Journal of Medicine* very appropriately and then there was an

editorial that went along with it that was written by Jeff Drazen, who's the editor, who talked about that one of the key lessons from this is what happens when patients and researchers get together and what happens is amazing things.

And one of the manifestations of that is that you get a publication in a major journal. And I won't be surprised if this then becomes, before too long, this may very well become standard of care in patients with LAM and hopefully will then lead to the next advance, which will better control this disease.

It's a great story and I have to say, I had an opportunity to talk about it at a meeting of the National Organization of Rare Diseases, but one thought that went through my head was, is that, why does this have to only be with rare diseases? Why isn't this with common diseases? We do see this with some common diseases. There's the Susan Love Foundation on breast cancer, it's a common disease where patients have come together to stimulate research, but I'm not seeing it with hypertension

and I'm not seeing it with coronary artery disease or atria fibrillation.

Wouldn't it be wonderful if we had that kind of engagement where patients were pushing the research community to get stuff done?

DR. WALLACE: David.

DR. MELTZER: So, two comments. Sometimes when someone says something that really matters to you, you remember where you were, and I remember being in a hotel room like this in Baltimore when I first heard Carolyn Clancy say, what's the receptor? You know, because it's this sort of jarring biological term in the context of something we don't usually think about biologically.

And I think that's really the key question, but I think it's a little incomplete, and the way in which I think it's incomplete is that research really rarely has a single receptor, it often has multiple receptors. And real change often requires multiple agents in order for it actually to happen. Doctors have to want to do it, patients have to want to do it, payers have to

support it, pharma has to produce it, all of these things have to happen together, and so I think one of the tools we need to get used to using is logic models, models that really describe all the sort of players involved, what we need them to do and how it is that the research that we're going to produce is going to move people so that things that wouldn't have happened, do happen.

And those are really hard stories to tell. You know, I guess my most striking experience with that is I was on the Secretary's advisory committee for Healthy People 2020 just a few years ago, and to summarize, there's no logic model. It really hadn't been thought through.

Now, on that committee we made a little bit of progress, not nearly as much as I think ultimately needs to be made, but I think this is something that if we could force grantees to really think through and gave them the space to do it, we'd produce much higher impact research.

I think it's a real blind spot still when we produce research. And, you know, journal

citations are one part of that, they're not the whole thing by any means. It's many, many more things than that and I think we need to start taking that seriously.

DR. WALLACE: Joe.

DR. SELBY: So, first I just want to say that days like today are really appreciated by PCORI staff, Board, and Methodology Committee, the kind of support and enthusiasm we feel from the patient and clinician and research communities really buoys us and to drag you into our deliberations, it gives us some comfort and some enthusiasm, so thank you. And I wanted to drag you just a little further into it, in fact, in response to Paul's question about where this is going and how will we know that we've achieved success, and it speaks right to why we are trying to prioritize to that really high value research.

In the legislation, we're going over this with a magnifying glass these days as we flesh out our strategic plan, in the legislation, believe it or not, it says that at some point, not clearly

specified, but you might read in that by 2017 when they decide whether to continue PCORI or not, Congress wants to see that PCORI research has been taken up and put into practice in healthcare systems, that it has changed practice, that it has reduced variation, and that it has reduced disparities.

So, that's five years, and you know how research goes.

DR. LAUER: Four years.

DR. SELBY: And we're also -- you know, this is not a thin limb that we're out on. I think it's a very firm limb and it's not going to break and we're not going to slip off, but we're out on limb saying that making research patient-centered, bringing stakeholders into the research teams, is going to make a difference in terms of the research being taken up, being more relevant, and when the results are out, if they're ready to be taken up, they are adopted, implemented.

So, this process is about, on the one hand, taking our best shot today at what would be

meaningful research, and then studying it carefully over time. Did having patients on the research team change the research from the perspective of, among others, the patients who were on the team? And eventually, was -- to what extent were these research projects successful in changing practices?

So, that's what the prioritization is about and those are the metrics that we're going to be looking at closely.

DR. WALLACE: Great. Well, let's -- maybe we should open things up. You know, the topic is prioritization, so it's really open for whatever you'd like to either comment on or ask about. And I think our first is right here.

MS. LUO: Hello, Michelle Luo from Baxter Healthcare. I really first wanted to thank PCORI for giving us the opportunity to be involved, you know, to really gaining a lot of insights of the prioritization. So, certainly it's not an easy process.

So, my question for the panel is that, you know, we already heard about a lot of different

stakeholders bringing different perspective, and on one hand, this is patient-centered, the initiative, so we have a lot of emotional needs, you know, if you will, from the patient, from the advocacy group.

But on the other hand, we also have to garner the scientific rigor and make sure it's going to be, you know, reducing uncertainty and can be implemented. So, I wonder, moving forward to actually roll out this prioritization process involving reviewers in the process, what's the thinking that for making a balanced decisions? And who will be actually the ultimate decision-makers in the process? And how does the process also encourage dialogue? If you do see diverging differences in terms of the view, how do you, you know, bring the parties together to reaching some consensus?

DR. LAUER: It's yours.

DR. SELBY: Okay. Well, I think you're talking about the review process that we apply when we receive applications more than the

prioritization process for the research ideas, and I do have something very positive to report to you and that comes from the first round of reviews, which just took place about a month ago, at which there were 30 percent of the study sections for each priority area were patients or other non-scientist stakeholders, 70 percent were the technical reviewers, and they were -- all five panels were chaired and co-chaired by very senior scientists who've shared many NIH and AHRQ study sections.

We were very curious about what the dialogue would be like in those sections, and they reported to a person that the dialogue was rich, that the scientists, as well as the patients and the clinician-stakeholders, really enjoyed it, got a lot out of it, and felt that it was to the point.

There was not -- we did not get reports of discrepancy between the views of scientists and the patients and stakeholders, and yet they felt that the presence of the others enriched it.

And I think it gets back to something that

I heard Dan Cherkin say just a minute ago that I am definitely going to remember, which is that, you know, patient-centered research is not about comparing two ways to treat a disease, it's about evaluating a decision that patients make.

So, we've seen this time and again. When you actually do say, we're here in the name of the patients to support decision-making by patients, it changes the playing field and it enables some of those conversations that maybe in another time and place wouldn't have gone so well.

DR. LAUER: Joe, my understanding is, is that you're not only using peer review as a tool to help you make decisions, but you're going to actually be doing research on peer review itself.

DR. SELBY: We are -- we very clearly intend to study things like -- just for one example -- how do the evaluation scores of the patient and stakeholder reviewers relate to the evaluation scores on individual projects of the scientists? And how do the various criteria like the criterion around patient-centeredness, which, as a number of

people have emphasized, is critically important when your evaluating grants, how does it relate to the overall score? Or is it like we typically see in study sections, it's all about the methods?

We hope that we do not want to undermine the methods at all, but we hope that we can see a signal of a relationship between is this patient-centered and what's the overall score.

DR. LAUER: And you're actually in a position, you know, because you're a relatively new one on the block, you're in a position to work with this and be flexible with this, and we've actually had some interesting conversations on this topic. And I've mentioned to Joe, for example, I was doing a review for another country's NIH, I was reviewing one of their big grants, and I was struck by the way they wanted me, as a reviewer, to review that grant.

They told me exactly what I was supposed to be looking for and then they actually told me that they wanted me to give up to 30 points for this item and up to 20 points for this item and up

to 10 points for that item, so they were making it very clear what they considered to be important. They weren't leaving it up to me.

And I was quite struck by that and I shared that story with Joe and I think, you know, we're in a position here where we could actually not only impact the research, perform the research that gets done, but also the way that these kinds of decisions are being made.

DR. WALLACE: So, Arnie, maybe you could comment. How does that look from the governance angel at PCORI?

DR. EPSTIN: Well, our -- I don't have anything useful to say.

MS. FLEURENCE: I have some --

DR. WALLACE: Sure, Rachael.

MS. FLEURENCE: So, several things. I think there are 35 pilot members in the room today and not all of you got to stand up on the panel, so if you did have information that you'd like to share, like, please also take the opportunity to do that now, so that would be great.

I think, you know, today we were really focused on the research prioritization process and, I mean, this morning it did get quite technical, there's a technical aspect to research prioritization, but there's also another aspect that we're working on, which is, how do we get these best questions to PCORI and, you know, for now we've opened the website, we're looking at a number of questions that other agencies have, but there's a lot of work to do to get clinicians and patients together so that we sort of decentralize the process of having them work together to get the questions trickling up to PCORI..

So, I think that's another big aspect of this process that we need to be thinking about as well and not just the sort of technical nature of what we talked about today, which is, once you've narrowed down that set, looking at each question individually.

DR. WALLACE: Yes.

MR. BASU: This is Anirban Basu from Seattle. I'll go back to David's presentation

about the value of information, and where he showed, based on some of our past work, about the value of understanding heterogeneity in subgroups could be quite substantial.

But often the problem of calculating the value is that we often do not have prior information on subgroups and heterogeneity. And I was wondering if the panel could comment on the possibility of funding maybe a series of small studies that would be primarily targeted towards generating hypotheses so that you would not only use that to prioritize bigger, future research, but also help in designing bigger studies, impactful studies?

DR. LAUER: Well, I'll just give -- this is my opinion, this is not the opinion of PCORI. It might be. But, you know, I think, Joe's only got a limited amount of time to work and he's got to show something, that's what he just told us, and the way you come up with definitive results that people are going to actually believe and may actually impact practice, is by doing large-scale

studies and huge numbers of people.

And it's possible to do large-scale studies and use numbers of people at remarkably low cost. It's being done, it's been done, it's not the typical model, but it's perfectly possible to do this, and that can have an impact very fast.

One of my favorite ones to talk about is the GSSI trail, which we talked about briefly this morning, which was a trial of 12,0000, it was done for a total cost of about half a million dollars or less, and that trial established, within 17 months, the trial took 17 months to do, and that trial established that thrombolytic therapy worked in acute myocardial infarction and within a very short period of time there was a dramatic uptake in the use of that therapy.

And then there was also work that was being done based on the results of that, looked at various subgroups to see whether or not certain groups of people did better than others.

If you want to -- you know, if he's going to have an impact and be able to show he's going to

have an impact, I'm not sure generating hypotheses is the right way for him to go. It might make more sense for him to take that -- there are lots of hypotheses that are out there, you know, it might make more sense to take the hypotheses that are out there and do some studies that are likely to have an impact answering those.

That's my opinion.

MR. BASU: But I would like to follow up on that because that might have worked in one instance, but in the context of CER, it's very difficult to see that you can do very large studies, RCD studies, because you have to think that these are treatments that are out there already funded and covered by insurance.

So, you have to think that why the patients would want to enroll in a randomized setting when they can access the same treatment outside our city free of charge. So, this is not some experimental therapy or new treatment that you are trying to randomize, these are treatment that are already used in practice.

DR. LAUER: Well, it's because they want to know the answer. So, there's, for example, a trial going on right now in Marfan syndrome and they're comparing losartan and atenolol, so these are treatments that are available. And the Marfan Foundation -- this is, again, where the engagement of the patients is critical -- so, the Marfan Foundation has come out and told their -- and communicated amongst the members, said, don't be taking Losartan unless you're in this trial, because we don't know what the answer is, and the best way to find out what the answer is, is to do a large-scale trial.

So, they want to know the answer and that's the reason why -- and this trial is done. It's now in the follow up phase, but they were able to enroll hundreds of patients with a relatively short period of time for a relatively uncommon disease, and the reason why was because they wanted to know the answer.

DR. WALLACE: I think you also mentioned the critical role of the Marfan Foundation --

DR. LAUER: Yeah, absolutely.

DR. WALLACE: -- that these third parties are really a critical piece.

MR. RAMSEY: I want to rephrase and maybe emphasize Anirban's comment in a slightly different way. Scott Ramsey from the Fred Hutchinson Cancer Center.

You know, in medicine, in our world of research, we often gravitate towards questions where there's clinical equipoise, where, you know, different stakeholders have different opinions, and there's a real question, but we often don't ask the question about patient equipoise, and whether patients are willing to go one way or another, and I think about this a lot in cancer because we've had many, many studies where, you know, I would think patients would change their ways. I mean, PSA, screening for prostate cancer, is a great example, and we just don't see that happening.

Now, one argument we could make is that patients just don't have the right information, we're not giving it to them in a way that they can

make a decision. The other is, is that the patients aren't going to change their ways and doing more research isn't going to change that patient's opinion.

And I just wanted to see what your thoughts were on this issue of patient equipoise and whether that's a useful criteria for thinking about prioritization.

DR. SELBY: I mean, I would say if we've got patients on the prioritization panels, that indeed, our aim would be to determine whether in fact there was patient equipoise or whether, you know, the patient view was that this is a settled question or not an interesting question.

MR. RAMSEY: But you have a real sampling problem. It's much easier to get that information from physicians and the health industry because it's all published. Patients self-select to be on the panels and we're grateful for that, but they may not represent the mass of opinion out there.

DR. SELBY: So, what you're suggesting has been suggested before that -- at some point before

you decide to go down a particular funding path, you actually survey patients in a much more representative way --

MR. RAMSEY: Is that feasible?

DR. SELBY: -- to see if that question resonates. I mean, after all, those are the questions we're after. So, I take your point.

DR. WALLACE: Does that imply other study designs too? I mean, so, I think you could argue, for instance, that patients like me sort of beings with patient equipoise and then seeks to, you know -- so, what are the implications of a focus on patient equipoise for the types of studies we'd be after?

DR. LAUER: One way of thinking about this is that a key issue for prioritization for us is feasibility, is, can we actually get this study done? And in this particular case, because the time window is fairly short, that is really important.

So, this might be a good way for you to assess whether or not your study is likely to be

feasible.

DR. HICKAM: I think it's also important to loop back to patient-centered outcomes. I mean, if we can understand which outcomes are really meaningful to patients, then I think it helps us to predict that the information will be useful.

DR. WALLACE: David.

DR. MELTZER: I'd like to go back to Anirban's question about hypothesis generation and just raise the possibility that there may be some opportunities to very quickly generate hypotheses that could be useful. So, for example, observational studies where you already have a cohort and you're very quickly generating hypotheses, that could be useful.

Another example is a very small pilot study of something that, for example, PCORI's thinking of studying but is unsure whether there's patient equipoise.

Despite our efforts, it's still really hard to fund those things. From the time an RFA comes out to the time that it gets reviewed to the

time it gets funding to the time you do it, despite, you know, NIH efforts to improve it, it's still really tough. And I wonder whether PCORI -- you know, I fully respect the pressure PCORI is under to get results, but I think that it might be useful in that context to think about whether there might be some activities of the type that Anirban mentioned that PCORI could put out an RFA for that would require results fast.

Our responsibility to the grantee is to review it and give them money within three months. Their responsibility to us is to give us the result within six or nine. And I don't know if that's possible, but if we could do it, it would be different, certainly, than anything we have now.

DR. WALLACE: Arnie.

DR. EPSTEIN: I'll speak not for the Board but of the Board, and for Gail Hunt, as well, who, as we were sitting here this morning listening to Gail Wilensky talk, it struck both of us that she was our advocate with one foot on the Hill and one foot in the research world telling us very clearly

that we had really put our minds to getting results first, second, and third, or that we'd miss an important opportunity, not only for patients across the country, but for all of us who care about that.

DR. WALLACE: Let me bring us back to Rachael's comment earlier too to remember about our core reason for being here today is to think about what we're learning about the prioritization process. So, we've talked a little bit about here what would we charter after we prioritize, but we want to come back a little bit too.

And there is a rich experience in the room either in past experiences with prioritization or with the current alpha test. And so, let me just see if there were other feedback or questions or comments about that process.

MS. WILSON: I think Alison Kalloo has a question and she was on the -- or a comment. She was on the pilot group panel, and this is Katie Wilson with PCORI. Later I'd like to represent a comment from Dr. Mark Flury that came through from the American Association for Cancer Research.

DR. WALLACE: Okay, why don't you go ahead, Katie, and then we'll come back over here. So, go ahead.

MS. WILSON: So, a very detailed but thoughtful question has come through, I believe it should be directed to Rachael Fleurence, from, as I mentioned, Dr. Mark Flury at the American Association for Cancer Research.

So, he'd like to hear more about the interplay of various prioritization processes at PCORI. So, he sees that there are at least three places where prioritization occurs: first, picking topics for targeted funding announcements, second, evaluating/prioritizing by review panels of a broad spectrum of submissions, and then, third, by the Board when rebalancing occurs.

So, he applauds the rigorous focus on the first type, but acknowledges that prioritization happens in each of these processes. So, with the targeted funding only being a portion of PCORI's overall funding, could you comment on the formal processes in play and the other prioritization, and

more importantly, the interplay between them.

An example: will topics prioritized for targeted funding be de-prioritized if they show up in open announcements because they are addressed elsewhere in targeted announcements?

MS. FLEURENCE: Thank you, Katie. We'll certainly not be funding the same question twice, so for sure there will be some sort of examination of our portfolio in that respect.

I think Joe explained quite well this morning that right now we have two processes. We have the investigator-led process, which is the more traditional process that we're used to from NIH whereby we reach out to investigators in the field and we let their best ideas come up to PCORI. Then this goes through a rigorous peer-review process, and in that respect, goes through some sort of prioritization as it's peer reviewed and then as it goes to the Board for final selection of studies to fund.

What we're talking about mainly today is the complimentary process whereby we go out to the

patients and stakeholders and ask them for their best ideas and so that these ideas trickle up to PCORI.

This process takes a bit longer because there's a lot of noise in the questions that we're receiving. There's also a lot of questions already out there, so it takes some effort to do this intentionally and to do this well.

In terms of the questions that PCORI has settled on so that the three that were mentioned this morning, which include uterine fibroids, fall prevention in the elderly, and, I think, the asthma question, these were PCORI's effort to -- we were told this morning to work fast and that was our way of looking at what we already knew in terms of questions and really working quickly to be able to get these funding announcements out to the field, so that process was a sort of fast -- a rapid process so that we could be responsive to questions that we know are out there.

So, there's a lot going on at PCORI at once. We are trying to be effective, and I think I

can see why to the outside world it may seem like we're doing a lot of different things, but we -- our prioritization is based on criteria that are similar and consistent and our mission remains the same, to fund research that's going to improve patient outcomes.

DR. WALLACE: Yes, Arnie.

DR. EPSTEIN: Yeah, I'd also cascade one level down in the prioritization process. You've really spoken to the first steps, which is, what are the targeted areas, but within those areas, we're going to draw priorities for individual proposals and in addition to the traditional criteria of excellence and transparency, I think we're trying to push the process in two ways, and this is certainly under the strong leadership of Joe and Anne.

One way to do that is to get patients centrally involved, and stakeholders, in the evaluation process, and the other is to shift even more -- not that there's a trade off, but sometimes there is, between internal validity and importance.

I think there's been a real effort to try and say, we really want to go where things are important, you know, so long as the methodologic standards meet a high level, let's choose the most important projects, and we're really moving in that direction.

DR. SELBY: I'll just add -- let me compliment that questioner. I mean, it sounded like they listened very carefully and understand PCORI at a pretty deep level.

In terms of the third type of prioritization they mentioned, which they called balancing, which is something the Board would do, we haven't done much of that yet. I think it's a very interesting question if, for example, we had a targeted funding announcement and we had funded four or five projects in a particular area and then something came through the investigator-initiated route, scored very highly. I think the texter or the caller is right that the Board, over time, is going to get more and more familiar with our priorities and they will have to take that into

account. But we haven't faced it yet.

DR. WALLACE: Great. So, let's see, I think we have a question back here, or a comment.

MS. KALLOO: Hi. Allison Kalloo, Clinical Ambassador. Thanks. This is a wonderful conversation.

Two things strike me -- well, first of all, we stand at the threshold of selecting life-altering research. Missing though, in my estimation, is the prioritization criterion of communication itself. Rather than putting the burden on the review or receiving end, clarity and transparency should rest on the shoulders of PCORI grant applicants.

In addition to it being a PCORI research area of interest, I think communication and dissemination should be made part of the selection toolkit across all topics, a filter by which the merits of research is prioritized, so systematically mandate and score clarity and simplicity.

This would speak volumes, I think, to our

ultimate ability to communicate patient-centeredness and would also underscore the PCORI mandate and slogan. I think it would also ultimately show us where the rubber would meet the road.

Research done differently is our slogan. Let's prove that. Research that cannot be discernable or simplified in this way should not be funded, in my estimation. The final assessment of this clarity, by the way, has to be made by patients themselves.

Secondly, and toward that end, I'm going to go out on a limb and submit that the medical community uses a different skill set and different language than those I fondly refer to as "real people." We communicate differently. This perpetuates the disconnect and a persistent inability to be patient-centered.

So, I'd like to see PCORI set a new standard, set a new bar, a new example of collaboration such that researchers partner with communication consultants, experts, creatives,

whatever you want to call them, or at least non-scientists, to mediate communication with end users, not only about outcomes, but about process, prioritization, and intent. So, prioritizing the art of communication is my plea to you.

DR. WALLACE: Joe.

DR. SELBY: That's -- thank you. That's really intriguing on several levels. The notion of telling our review panel to -- telling our applicants that they should write in as clear and transparent and simple language as they can will still getting their points across and telling our reviewers to score on that, is an interesting notion.

I'll tell you a couple of other notions that have come up. One is, we had this large patient stakeholder meeting here in late October and patients stood up and said, you know, patients should write a portion of the application, those patients that are going to be on the research team ought to be writing a portion of the application, and I think that's an intriguing notion.

The third thing is, there is this -- I'll stop with this third one -- there's one caveat that is we are just as dependent as we are on patient-centeredness, we're also ultimately dependent on the quality of the research methods. So, there is some tension, probably, between making things simple and readable and really communicating to the reviewers exactly what they're going to do with the methods so that they can evaluate whether the research has rigor.

So, I just put that out there as probably a bit of a tension sometimes in some parts.

MS. KALLOO: I just wanted clarification, I wasn't suggesting [off microphone].

DR. SELBY: Yeah. It's just that sometimes there might be a little push and pull.

DR. WALLACE: Great. I think back here with the microphone.

MS. MUKAMEL: Dana Mukamel from UCI. I participated in the pilot process and, first of all, I want to say that the criteria that we used, I think, are right on the mark. They made a lot of

sense and I think really captured a lot of the important concepts that should be captured and I really applaud PCORI for putting together a set of very thoughtful criteria.

But I think the real challenge is to operationalize them, as we heard throughout the day.

Two of the criteria that I had the most problem with, I think, tied to what Dr. Epstein talked about beforehand and that's finding those areas of those topics where the big potential for improvement is, and those are the criteria that deal with the most potential for benefits and the most potential for reducing uncertainty.

So, I spent a lot of time trying to think about it, and in particular with respect to the information that we were given with the ten specific topics, and what I found was happening was that I either -- and this may have more to do with how I think about things and perhaps other people didn't have the same sense, but I felt that I either had a lot of information and ability to

answer that question and in those instances, I asked myself, well, if there is so much information, what is there left to research. Or else there wasn't enough information and then I said, well, I can't answer the question.

So, I really was sort of in a conundrum, and where I ended up was feeling, I'm not a clinician, I'm a methodologist and a health economist, and my sense was that the people who are, perhaps, in a position to answer that question would be clinicians and perhaps specialists in that particular area who might have a gestalt and therefore would be able to, just from the general knowledge of there, be able to answer that question. And that got me to thinking that perhaps there are some criterion -- those two ones are very important in my opinion.

So, perhaps the way to address it is that some criteria should be addressed by specialists in the area and some criteria might be better addressed by other types of stakeholders.

DR. LAUER: So, you're saying that there's

a need to bring in specialists who would be able to provide a sense as to how great the degree of uncertainty is? Is that what you're saying?

MS. MUKAMEL: Right. That research might actually address the question -- research might reduce the uncertainty.

DR. EPSTEIN: It's actually a friendly caveat. It's not only the level of uncertainty, it's the extent to which research is capable of reducing the uncertainty.

MS. MUKAMEL: Right.

DR. EPSTEIN: Which is slightly different.

MS. MUKAMEL: Right.

DR. EPSTEIN: I think what you just said is 100 percent right on target. It's exactly right. There has to be another layer of clinicians who can say, in so many words, what's changed. We've known about this being an important area for 20 years. What makes us think now that an infusion of resources from PCORI could make a difference? And getting that information and choosing wisely is one of the many tasks we have. There are others,

it's got to be patient-centered and other criteria, but that's clearly an important ask.

DR. WALLACE: Great. Thank you. Let's see, Bobby?

DR. DUBOIS: Bobby Dubois, National Pharmaceutical Council. I'm a very practical and sometimes blunt guy, so, Michael, you raised, and multiple people have said, oh, well, PCORI's got to demonstrate improvements quickly. How about just taking a certain percentage of the money and forget the prioritization process? Do an RFP for we need quick results that are demonstrable, back to the GAO, and we want RFPs that address that. Why are we talking around the issue instead of directly asking -- and I suspect every researcher has some creative ideas about what they think they could do quickly to demonstrate change.

DR. EPSTEIN: There's only five minutes left and you bring it up now? I feel like you just gave the answer.

DR. SELBY: Saved the day.

DR. EPSTEIN: I think it's a very

interesting idea, Bobby, really interesting. We'll see that it has legs.

DR. WALLACE: Well, there's nothing that would preclude that surfacing through the other pathways too, right?

DR. EPSTEIN: Yeah, yeah, no, but it's an interesting idea if what we're all about -- and we're trying to say is an important mission is to get something out there, why not get the help of 300 million people around the country?

DR. WALLACE: Let's see, I think over here.

DR. WEISMAN: Harlan Weisman. The last set of questions or discussion about experts reminded me of Dan Cherkin's answer to me in a very eloquent way about why PCORI is different and Liz said that she considers herself a social scientist over some of these kinds of issues, but some of the things that are important to patients beyond the diseases or what they think is important is their personal sense of well-being. Some of that is their physical health, some of that is their mental

and emotional health, and some of that is their spiritual health, not necessarily in a religious sense, but in a sense of meaning, purpose, of value of life.

Do you think, Joe, that in our study sections or in -- even in the prioritization of what we're doing, that we have adequate representation of social scientists and others who know far more than physicians or others -- you know, and again, Kirk talked about the fact that we need other than physicians and maybe more classic clinicians, you know, like occupational therapists, but I worry that when we say the study section and we talk about the experts, we're talking about scientific medical experts, but not necessarily people who know how to attend to these other realms of well being.

DR. SELBY: Well, both Kirk's comment earlier and yours have made me think about that -- that the scientific portion of the study sections is made up of people who responded to our call for scientific reviewers. About two-thirds of them

have done review before, one-third of them had done reviews at, for example, NIH or AHRQ, one-third hadn't.

There were a lot of social scientists on that list, I can tell you that as well as clinicians, but, you know, whether they were -- I don't think there were very many physical therapists, so Kirk's point was well taken and I want to go back and look at that. But I think your point also is, do we have people -- and carefully placed on each study section -- to think about, particularly about the patient's perspective here.

DR. LAUER: Paul, I have an answer to Bobby's question. John Ioannidis, who's a member of our Methodology Committee, wrote this terrific paper a number of years ago called *Why Most Published Findings are False*, and he had a table in there about, you know, what kinds of studies are most likely to be true, because ultimately for something to have an impact it has to be true.

And the studies that are true are large, they're randomized, there's pre-study equipoise,

and there's minimal bias, and those are the kinds of studies -- and we've actually hit upon all of these in this discussion, that there's equipoise ahead of time, and they have scientific rigor. And, you know, maybe if we take another look at that, and think about it that way, that it's a very nice, elegant way of thinking about what is likely to produce research which is going to be true, and therefore believable, and therefore likely to have -- more likely to have real impact?

DR. WALLACE: Let's see, we have a question right here.

MS. MORGAN: So, hi. I'm Linda Morgan. I'm a patient representative. I have Parkinson's disease and have done a lot of clinical trials --

DR. EPSTEIN: Can you talk in --

MS. MORGAN: Am I talking? Yes, yes.

[Laughter.]

MS. MORGAN: Sorry, that's one of the side effects of Parkinson's. So, I'm a patient advocate, have Parkinson's disease, and have done a lot of clinical trials, and so I've had my hand

raised a little bit so I have different points. But, first of all, on the quick -- go out there and ask for the quick research, quick turnaround. In addition, we want to go to the patient advocacy groups and just ask for the top three in each group, you know, Parkinson's what are the top three questions, cancer, what are the top three questions, et cetera.

But what I really wanted to say is to your point, Michael. There are a lot of patients out there that are exactly what you described, that want to be involved and that go to -- you know, if they had the opportunity, would be involved, except this is as somebody else mentioned, this is a very interesting group of people. You know, I'm amazed in that everybody's patient-centered, obviously, right, that's what brought us here, but that's not how it is across the country. You are a unique group, is what I'm trying to say.

So, that when I go with my interest in being involved as a patient and making a difference in research and research questions, I go to my

people that I've done clinical research with and say, I want to be involved as a patient. They're saying, well, what do you want to do? Do you want to be in this trial? I said, no, I want to help you come up with the questions. I want to disseminate the knowledge, I want to help with the analysis just from my small standpoint, and they don't have a clue what I'm talking about.

So, I would ask you all to go out into your groups, go forth and multiply, go forth and tell your individuals that you work with that -- how important patient-centered care is and help that grow in the country.

DR. SELBY: If I could just say briefly, that one of the things we have going for us here is the money that we have to give out and the fact that the kind of researchers that do this research don't have a whole lot of other sources, other sources of funding are flat or shrinking a bit, so there's a lot of -- we have encountered an amazing amount of interest and curiosity and even some concern in the research community about the extent

to which we are pushing researchers into partnerships with patients, but they're learning, I mean, they're very curious about what we mean.

Somebody asked us a couple days ago, how many patients do we need on the team to make it a good application? So, the leverage of funding is beginning to have the effect you hope to see.

DR. WALLACE: Yes, over here.

MS. HUNT: Hi, Deborah Hunt, nursing professor from the College of New Rochelle. First of all, I'm just so grateful to be involved in this because it's been a wonderful experience, but as I've been listening to everyone, and it's all been really helpful, one of the things I thought about is in the hospital we have inter-professional teams, and someone talked a lot about occupational therapy, and really, we need all the stakeholders from the clinicians -- so, the physical therapists, when we have -- the hospital I'm in now has daily rounds to talk about that -- every single patient, and it's the pharmacists, the physician, the nurse, the nurse manager, the occupational therapist, the

physical therapist, the nutritionist, so that whole team.

And of course, I don't know all your inner workings yet, but I think it's important because we look at patients holistically to make sure that all of those other professionals in those disciplines are also involved in this process, because they really do look at all -- that holistic patient. So, thank you.

DR. WALLACE: I think we have the yellow light, which is a sign that we're approaching the break, that's good news, and I wanted to first of all thank our panel, and I hope you'll join me.

[Applause.]

DR. WALLACE: And we will have a 15-minute break. Maybe just as a transition comment, what strikes me is that we're dealing with a really complex issue and complex issues have to be solved along two different dimensions. You have to create increasing certainty, but you also have to create increasing agreement.

And one of the consistent feedback that I

hear is that the number of stakeholders and the involvement of stakeholders has expanded significantly.

We've talked about teams at every level from the research team, and we thought about how challenging it is to involve the patient, but it's also challenging to involve people that can communicate. We've thought about the evaluation team and the importance there and we're increasingly, I think, going to think about the accountability team and how we see down the road what the actual impact is of these things.

So, I think that there is a creative tension, but I think, again, the panel, and really the whole day, has modeled well the pursuit of increasing recognition of the team members and the critical players.

So, we'll take a 15-minute break and when we come back Joe and Rachael will share with us the path forward. So, thank you.

[Recess.]

MS. FLEURENCE: Hi, everyone. We're just

going to wrap up today with some thoughts and learnings from what we heard from all of you today, both from the expert methodologists and from our panel and from other folks in the room.

So, you know, we'll be fairly brief. I think we heard themes and feedback in two big areas, one is in the science of prioritization, and we heard these excellent presentations this morning on the actual methods for doing research prioritization. So, from a practical point of view, part of our task at PCORI is going to be to figure out how to weave these techniques into our process keeping the rigor of the science, but at the same time making these both accessible to folks using them, and also to make these -- to be efficient in the process, because it seems to me that some of these methods will take up quite a bit of time that we don't have.

So, that was one big area that we heard about, the science of prioritization, and then the other big area that we got feedback from was from the folks, the patients, the stakeholders, who

participated in our process and all the really useful information we got on what does it mean to bring a diverse group together to work on a prioritization process, and is -- you know, I think for us is what's it going to take for PCORI to be successful to be able to get useful research funded quickly, to be able to get results quickly, and to be able to show where this research is improving patient health outcomes.

And so, I'll turn it over to Joe for some more precise points that he's taken throughout the day of ideas and feedback that we've received.

DR. SELBY: Okay. Thank you, Rachael.

Well, I'm going to start with a Tweet that was up here just as I was walking up here I saw it and now it's gone, and it said, VOI sounds like a very promising approach, now you just have to make it understandable to mere mortals.

And, you know, that was a little bit the way I was feeling still, even though I've heard it several times before, and I'm convinced that it is rich and that it's got the right ingredients. I

think a lot of people have confirmed that the ingredients that go into VOI, this notion of the amount of uncertainty that there is, the current practice and how much that might change and what that would do in terms of changing outcomes, the durability of the effect, for instance, those are critical measures and as the afternoon wore on and we heard the reports back from the pilot projects, my optimism grew that we are, in fact, going to be able to take those key concepts and put them into measures and topping briefs, if you will, that preserve the value of those ideas, but in a clearer, more understandable package.

So, I'm optimistic.

I'm going to just go through a number of comments that I heard throughout the day that I think are going to be very helpful for us as we go back to the office and evolve this to the next level, and I predict that PCORI's prioritization process is going to continue to evolve. As long as we live, it will never be fixed or permanent, but I'll also predict -- this is really going out on a

thin limb, that it will one of these days be known as the most ambitious and the most successful prioritization process on the planet because it really does go through the very hard work of considering topics across such a broad range.

So, we're going to stay at it with your patience and your ongoing support.

I really liked a comment that I heard from Andreas Laupacis this morning. He asked David and Claire when value of information analysis is really needed, and I think the suggestion was, sometimes you don't need something so sophisticated, but there may be other points, like when you're contemplating spending $10 million when it's worth taking more time and doing the careful analysis.

David also, and Claire, and Karl from his text message, suggested setting aside some money and getting these topics available a little bit ahead of time so you have time to do that. I think all that's going to be very helpful to PCORI.

The notions that several people -- I know Dan raised them, but others too, about -- and

Anirban raised them, I believe, about patient-centeredness and is it applicable to research ideas or is it applicable more to applications, to actual proposals. I sort of -- my thinking changed during the day and at the end I think the aspects of patient-centeredness which are available at the research topic idea, and one of the best measures there is, are patients asking for this? That notion of survey the patients and see how this resonates with them. Are there patient advocacy organizations that have identified this as a high priority themselves?

So, that aspect of patient-centeredness counts at the research topic level, but did they get the question exactly right and did they get the right outcomes? That's more a function, I think, of the individual study.

I also came away thinking, are we going to have to expand the responsibilities of these panels a little bit to build in some thinking about what study designs would answer this question. It certainly has to do with the costs of the study

and, as you saw, costs actually go into a real formal VOI, so the cost of the study, so, I think we may actually have to prevail on these panels to think a little bit about study design. Another interesting notion is, sometimes it takes more than one study to really change practice, so we may have to discuss, is this the kind of thing that should have two, three, four studies, or maybe a little bouquet of a randomized trial and a big observational study? We may put those questions to the panel.

I agree with Ronnie Goff who said that -- and so I'm backtracking on something I said up from the slides this morning, which is that if we see some kind of incentive that would make it hard to get this finding implemented, even if it came out the way we thought, that we might move the prioritization down. I completely back away from that. We'll just break down the barrier when it comes time, with Ronnie's help.

The idea of setting aside a pot of money for rare diseases makes a lot of sense. The idea

of setting aside another pot of money for quick hits -- Bobby's idea from a few minutes ago, also deserves careful thought, so thank you for both of those.

Also, Ronnie had a comment about the prioritization process really needs to factor in, is there any research like this going on elsewhere, and I'll say that that's actually kind of part of the gap confirmation process, so, we do intend to factor that in. If there's another study underway or about to get funded by NIH or anybody else, we'd want the panel to know that.

I'm also going to just say here for the first time today that PCORI is going to be very interested in co-funding, so if there's opportunities to co-fund projects, that enables us to spread our resources more broadly, maybe influence the way other funders do their research to agree that they make it more patient-centered, like the idea of that, and we'll think hard on this, that panelists -- ideal panelists often bring multiple perspectives, perhaps clinician-patient or

clinician and caregiver, although we also heard that you can't let this slip into a situation where you don't have people who are primarily here representing the patient perspectives. So, both of those were important.

Somebody asked, is PCORI ever going to be a generator of ideas instead of just a recipient of ideas, and I think unless you're Einstein, you probably don't really generate all that many ideas, you probably -- they probably gradually come into your mind as a process of interactions, but I think that sometimes the ideas will appear in our minds first because of interactions we've had, and those will make it -- I guaranty you, we will get our ideas onto the list that gets prioritized.

So, that's that.

The notion of patient equipoise, I think, is really a nice new idea. Perhaps some idea of surveying real patients, a broad, representative sample of real patients, occurred to us before, but you reinforced it today, and it would be a really useful piece of information if not for the

prioritization panel, for the Board before they decided to, yes, go with this high priority topic.

And then I can't leave this page without going back to the suggestions from Allison about scoring applications on the clarity of their communication. So, this will drive the research community even crazier than putting patients on the research teams, but that's -- I'll go back to Michael Lauer's suggestion that if you -- Tony Fauci's suggestion that if you don't piss somebody off each day, you're not doing your job.

And the last two comments -- Rachael, I'm just about done, I promise -- these are two comments that came via Twitter. One was just reminding PCORI that we need to attend to patient needs in the research prioritization process. I think this is the same idea that we've mentioned a couple times now that these are -- these research questions are supposed to address decisions that are faced by patients, not just comparisons of two treatments. That is not really a need that patients have.

And the last one was -- hasn't been discussed here today but we've discussed it in other settings so I'll mention it. The comment goes, democratic nature of funding, small observational studies with quick turnaround could point to larger studies by patient researchers, so I think they're saying, sometimes patient researchers -- we should bring patient researchers along with small grants.

And we've actually talked in that October meeting I mentioned about the idea of micro grants, about a program of small grants that are meant mainly to get patients and researchers together in various geographic -- in local areas to begin building research teams and to begin identifying the right questions for their research.

So, micro grants is something that we're actively considering.

And with that, Rachael, I'll stop and turn it back to you.

MS. FLEURENCE: So, I just wanted to close with thanking everyone and just saying, we're going

to be using the feedback that we've received today to finalize our version 1.1, I guess. We're a learning organization, so what comes out in January will not be our final iteration. We'll keep learning from what we're getting back from our prioritization panels, the way we've learned already from all of you over the past few months and then today about how to make this process work so that we can achieve our goals.

So, with that, I wanted to just thank everyone for coming.

DR. SELBY: And, Paul, did you have anything you wanted to say as we close? Okay, then, I think I'll just add my thanks, first and foremost, to all of you who went through this pilot process. That was brutal; actually, I think we all know in retrospect that we asked a lot of you, we knew it even going into it. Thank you.

Thank you to the Board members, the Methodology Committee members who participated in this today. Thank you to Rachael and Katie and Natalie for all the work you've done on this, and

to all the staff of PCORI who helped us with today.

And stay tuned. I guess one of the things you should watch for is announcements about the formation of the advisory panels. Some of you may actually want to apply. You can imagine it's going to be quite a diplomatic set of endeavor to populate these first four advisory panels. But we'll do it. And thank you.

[Applause.]

[Whereupon, at 4:05 P.M., the workshop was adjourned.]