PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

BOARD OF GOVERNORS MEETING

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[Transcribed from PCORI teleconference.]

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Allen Douma, MD [via telephone]
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Christine Goertz, DC, PhD
Leah Hole-Marshall, JD
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Robert Jesse, MD, PhD
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Richard E. Kuntz, MD, MSc
Sharon Levin, MD
Freda Lewis-Hall, MD
Barbara J. McNeil, MD, PhD
Grayson Norquist, MD, MSPH [Chairperson]
Ellen Sigal, PhD
Kathleen Troeger, MPH
Robert Zwolak, MD, PhD

AGENDA

AGENDA [Continued]

P R O C E E D I N G S

[9:08 a.m.]

DR. NORQUIST: Good morning. I'm Gray Norquist, Chair of the PCORI Board of Governors, and I want to welcome you to today's Board meeting, which is being held in Washington, D.C., as well as via teleconference and webinar.

For those unable to attend in person, instructions for logging in or calling in are available on our Web site at PCORI.org/event.

All Board members are present with the following exceptions, Allen Douma, who I think is on the phone.

I want to remind everyone that disclosures of conflicts of interest by members of the Board are publicly available on PCORI's Web site, and are required to be updated annually. Members of the Board are also reminded to update their conflict of interest disclosures if the information has changed. You can do this by contacting your staff representative. If the Board were to deliberate or take action on a matter that presents a conflict of

interest for you, please let me know so we can discuss that or address the issue.

All materials presented to the Board for consideration today will be available during the webinar and then after will be posted on our Web site, PCORI.org. The webinar is being recorded and the archive will be posted by the end of the week.

We have a scheduled public comment period today from 4:45 to 5:15 p.m. Eastern Daylight Time. If you are interested in registering to provide public comment, please visit our event page for instructions, or you can always e-mail us at info@PCORI.org, or provide input to the Web site.

Final reminder, we are live putting today's activities on Twitter, and you can join the conversation at PCORI.

At this point, I think the first item is the minutes, approval of the minutes.

So, people should have seen the minutes, and I just need to know if there are any comments, corrections, edits.

SPEAKER: So move.

DR. NORQUIST: We have approval from Bob. Second?

SPEAKER: Second.

DR. NORQUIST: Thanks. All those in favor?

[Chorus of ayes.]

DR. NORQUIST: Any opposed?

[No response.]

DR. NORQUIST: Any abstain?

[No response.]

DR. NORQUIST: Okay, so first up is Joe Selby, who is our Executive Director, will give his report and Q3 Dashboard review.

DR. SELBY: Thanks, Gray. Good morning, everyone. Lovely to have a full turn out with Allen here by phone. This is the beginning of PCORI's seventh year, and six-year terms of Board members. The initial set for those six-year terms have come to an end, and that means we have some transitions.

To start with, it is a real pleasure to welcome two Board members, Dr. Russ Howerton, who is the Chief Medical Officer and Vice President of Clinical Operations at Wake Forest Baptist Medical

Center. Russ takes the place of the hospitals' representative on our Board.

Kathleen Troeger, who is Director of Outcomes Research at Hologic, Inc., joined PCORI as a representative from industry.

We have had a chance to talk by phone over the last few weeks, and we had an orientation dinner last night, and I think we have two outstanding additions to our Board. Welcome to Russ and Kathleen.

[Applause.]

DR. SELBY: Now, for the sad part. This has actually already happened, and we sort of said goodbye to Steve before and Harlan was not there. We are going to hear, as you know, a little later that Steve is coming back. We are saying goodbye to Steve Lipstein and also Harlan Weisman.

Harlan really distinguished himself when it came time for PCORI to do its first plan to set up its metrics, the Dashboard is a direct product of Harlan's advice among others, but Harlan really stepped up and brought his years of experience doing

strategic planning to us just at the right time.

Harlan, I want to say what a pleasure it has been working with you these years, and how much your spirit will live on and your contributions will live on as we move ahead. Thank you. We will get to thank Steve when he arrives.

Speaking of thanks, here are five members who decided to re-up. Each one of them have made remarkable contributions, chairing committees. Everybody here has chaired a committee during their first six years, and several of them are still chairing committees going into the second six years. For your willingness to stick with us during this next period of time, we all owe you tremendous thanks.

Christine Goertz, Sharon Levine, Gray Norquist, and Gray, I understand you have agreed to stay on as the Board Chair as well, and that is wonderful. Ellen Sigal, and Bob Zwolak. A hand for these folks.

[Applause.]

DR. SELBY: Also, we are having a couple of

transitions that are noteworthy and I want you to be aware of. The first is Dr. Romana Hasnain-Wynia, who joined us in October of 2012, and was the first program director for the Addressing Disparities Program. I don't think Romana is with us. I just want to say that Romana really brought an amazing background, a ton of energy. She has built a crackerjack team in addressing disparities, has awarded over $200 million to projects in this area.

I would be sadder if it wasn't for the fact that Romana is going to an absolutely wonderful job. She is going to be the Chief Research Officer at Denver Health, the nation's leading safety net hospital. She will direct a program of research including disparities research.

Denver Health is also part of PCORnet. I think we will continue to have a connection with Romana through PCORnet at Denver Health. Really, a wonderful next step, they are fortunate, we have been very fortunate to have Romana with us for these last four years.

Next, and this is kind of unbelievable,

too. Sue Sheridan, who has been the face of patient engagement since extraordinarily early on in PCORI's life, she joined us in February 2012, so she is approaching five years, and has been the Director of Patient Engagement that entire time.

I think it is really fair to say Sue's leadership style has a unique quality to it, which is very easy to embrace, it makes everyone feel comfortable, and she really put her mark on this organization by making sure that patients have been involved in everything that we do.

Can't quite tell you what Sue is going to do next yet, but I have a clue, can't say what it is, but it is extraordinarily exciting, and it plays to Sue's lifelong passion for patient safety and reducing medical errors, starting with experiences in her own life.

She really has made her mark for decades in this area and will continue to do that, and I know that we will continue to see much of Sue. Sue, I think you are here.

[Applause.]

DR. SELBY: It's tough to say thanks to all of you with the force that it deserves, but we are grateful.

At the end of 2016, starting 2017. I said at the beginning of 2016 we often like to name our years, something like the year of the rabbit, but we said this was going to be the year of refinement. There was a sense in which 2016 was a bit of a plateau. We got there. We looked around. We saw that a number of things could be improved, and in many areas, we spent 2016 improving these, with intense help from the Board.

The SOC worked closely with us throughout the first half of the year on enhancing the application process. Those enhancements that were recommended, half of them have been implemented with the last funding cycle in August, and the rest will be implemented in February 2017 with our next cycle, but we have streamlined and harmonized applications.

The goal was to make it more coherent and easier for applicants to use. I can say the application link will decline from 25 pages to 12

pages in February 2017. Thank you, SOC.

Similarly, with merit review, a remarkable effort, SOC and staff working together on merit review. To our merit review panels, we have added an additional scientific reviewer, working hard to ensure that methods expertise is always there as well as clinical content expertise.

We have done some aligning of PCORI criteria to make them somewhat more consistent with others while preserving our focus on engagement and patient-centeredness, work to improve summary statements and streamline the entire process.

The new two concepts, which one you will hear about later today, the idea of sequential targeted PFAs, if we have made an investment in an area, we may find there is other work to do in that area. Really, we owe a lot of thanks to our new Chief Science Officer, Evelyn Whitlock, in these two concepts, sequential targeted PFAs, and also specific set-asides within the pragmatic.

Yes, we have a list of high priority topics. With each cycle, we also emphasize areas of

special interests in the pragmatic trials. Those are two concepts that I credit Evelyn with introducing into the PCS portfolio.

The budget preparation for 2017, I think, was a collaborative effort of staff, the FAC, and all the strategy committees, the best budget preparation ever to date.

Lastly, and you don't probably know a lot about this, if you were on the FAC, you know something, we developed 150 policies at PCORI during the last year. It may seem excessive, but in our judgment, it was necessary. It really helps to upgrade the work experience, particularly helpful when new people are coming on to jump into the flow quickly.

One hundred-fifty policies, 250 standard operating procedures, and 50 guidance documents. A tremendous amount of work we were able to do because we got to a plateau. The last things we are doing in 2016 are setting the stage for 2017, which I can say is going to be a year of research results and dissemination. You will hear a lot about this today

and into 2017.

The peer review process has been fully implemented. I want to spend a little bit of time on that. Thanks to the work of a number of staff and led by Hal Sox and Marina Broitman, the peer review process is now in place. Just in time for the results, which are starting to come in in numbers, and in this next quarter, will begin to come in in large numbers. Our process mandated by the legislation is in place.

2017 will be the year in which we really begin doing both evidence syntheses and research dissemination. We hear a lot particularly in discussions about PCORI's accomplishments and whether PCORI is going to be renewed, we hear conversations about products, and whether PCORI is going to produce products.

We have research coming in now, and the next task is to synthesize that evidence, to go out and get other evidence that can be added to the research we have funded, and to produce products that are useful to patients but also clinicians and

payers, and you will hear a report from Evelyn on aspects of this later this afternoon.

I want to say a word about open science, open data, and transparency at PCORI. We have never really talked about these three policies together at the same meeting, but it is the combination of them that really I would argue puts PCORI in a lead role in terms of pushing the concepts behind useful science and open science.

The first policy is the peer review policy, which calls for immediate registration of any project, trial, or observational study on ClinicalTrials.gov. A month later, we post a summary on PCORI's Web site translated for a lay audience. We require submission of results consistent with NIH regs and FDAAA regs.

We require submission of results to ClinicalTrials.gov within 12 months of the primary completion date. We post an abstract with the results to our Web site within 90 days, a lay abstract and a scientific abstract, within 90 days after our peer review is completed, and the posting

of the full final research report. I don't think anybody else in the U.S. does this at this time.

We require a full final research report to be posted on our Web site, searchable in Medline, regardless of results, regardless of whether there have been publications, no later than 12 months after the final report has been accepted.

The second is our open access/public access policy. That simply says all final manuscripts must be deposited in PubMed Central, the manuscripts, and that PCORI will ensure that the primary publication from every study is funded to be published open access.

If the article has been submitted and accepted by a journal that does not have full open access, we will cover the cost of making it open access or public access on day one, so there will not be a delay between when it is published and when the public can see the primary publication from any PCORI funded study.

The last is the draft data sharing policy. You will be hearing a little bit later today from

Jason Gerson about a data sharing policy that we have been iterating with the RTC for the last 6 to 9 months. This policy is still fairly in draft in the sense that we are leaving some details open for public comment.

In it, we require the posting of initial and final study protocols. We require all projects funded by PCORI to prepare for data sharing and to have a data-sharing plan.

For large studies, pragmatic clinical studies, targeted studies, and for perhaps a select set of the smaller studies, PCORI will require deposition of the complete data package in one of several PCORI suggested data repositories, and cover the cost of transfer and storage.

We're going to ask you this afternoon to approve the posting of this draft policy for public comment, and we are confident that there will be a lot of feedback that comes from this public comment.

We have already gotten some wonderful feedback from the NIH, incorporated what we could, and held on to the rest to be merged with the other

public comments. That is coming this afternoon.

Just a word about peer review, where we are. We have now the final research report instructions. They put a strong focus on engagement and methodology standards, so researchers have to address those two. The outline is broadly similar to a journal article, meant to encourage the use of the final report as a submission to a journal. It includes subheadings for method sections.

There is another section on how patients and stakeholders were engaged, and there is an addendum for the authors to describe how they adhered to the methodology standards.

We have an online system for submission, and we are now accepting draft final research reports. Editorial Manager is that system, and it is used to manage peer review. We do this in concert with OHSU, which is the winner of the competition to play this role. We are also integrated with the PCOR Translation Center, which takes the final reports and develops the lay abstract.

Reviewer recruitment is underway. We have associate editors who have been identified by OHSU and trained to work with different types of reviewers because we do have patient and clinician reviewers.

Just to show you that we expect to have 43 draft final research reports by the end of this calendar year. We already have 12 draft final research reports that are in peer review. We expect to post the abstracts from these peer review reports starting early 2017.

If you remember the pilot projects, we have 47 out of the original 50 that have completed abstracts that will be posted before the end of the year. These are lay abstracts describing the 50 pilot projects.

Speaking of evidence synthesis and dissemination, Engagement and Science held a meeting with all stakeholder groups, 40 plus stakeholder groups, on October 14, and the aim was to discuss the needs of stakeholders with respect to evidence synthesis and dissemination tools.

The basic messages were stakeholders really want clear, concise, actionable findings. They want the bottom line at the top. They want a headline, not to have to read through 200 to 300 pages to get to the conclusion.

They encouraged us to work with trusted intermediaries, and they named particularly the Mayo Clinic web site and Consumer Reports as trusted intermediaries to think about working with in our dissemination activities.

They said please concentrate on areas where there is in fact is new information and clear evidence, always think about shared decision making and tailor the material to the audience. Reports of insufficient evidence to most stakeholders have little value, so don't spend a lot of time restating that there remains insufficient evidence in an area.

This was good guidance to get started, and we will have some of our first dissemination products within the next several months.

Last thing, just a reminder, the annual meeting is just about two weeks away, just over two

weeks from now. It is here at National Harbor. More than 1,000 members of the PCORI community have registered, four keynote speakers will start with a focus on patients and the patient's role in research. We will then move to how patient-centered research can support patient-centered care. We will talk particularly about patient-centered research in the area of complex and multiple chronic conditions.

Finally, a very interesting presentation from the just stepping down president of the Robert Wood Johnson Foundation on the relationship between patient-centered research and the community, community-based participatory research.

A very interesting session. I know a lot of you have roles moderating the panels or breakouts. We look forward to spending those three days with you.

I'll stop. Those are just some opening comments and touching a few faces that needed to be touched. Let's see if there are any comments or questions.

DR. NORQUIST: Francis, and then Barbara.

DR. COLLINS: Joe, thanks for that summary. I'm curious to know with regard to the public access policy which PCORI announced back in April, requiring that publications appear without delay, not just the 12 month period which is standard for everything that NIH supports, but it has to be in the public domain where people can access it and look at it.

That is clearly a direction that many of us think this whole effort should be going, but it's not without controversy.

I'm curious to know to what extent you had push back from publishers, and also whether you have had push back from any authors who discovered that the journal they really wanted to send their paper to didn't actually have, even with payment, an immediate access model. So, how has that been going?

DR. SELBY: We have had discussion with journal editors. I will say, Francis, I think there is built in tension. There is just a natural tension between wanting to get a full report out and

wanting to get papers published.

My priority is papers published, simply because they are a much more effective dissemination tool than a final report on our Web site will ever be.

What we say is as soon as the final report has been peer reviewed, we post a scientific and lay abstract of the final report on the Web site. There is then a period that can go up to 12 months. We will push at all times for it to go sooner, but we will do it with an eye on publications. We will also build into the whole peer review process a pressure to get the publication submitted at the same time the final report is submitted to us.

DR. COLLINS: I'm actually asking a different question, which is when that publication is actually accepted and it is going to come out in a journal, PCORI now says as of April that you want that published paper to be immediately accessible to everybody, without a 12 month delay, before it becomes visible in PubMed Central, and you are willing to pay the cost for publication in order to

make that public access happen immediately, as soon as the paper is actually published.

The Gates Foundation has now announced they are doing a similar thing, and it becomes effective in January. Wellcome Trust is looking at this.

Traditionally, as you probably know, many publishers, many of them actually supported by scientific societies, get very anxious about this because they fear this is going to erode their journal subscription income, because libraries won't need to pay very hefty subscription fees of the journals if everybody can see all of the published literature immediately online anyway.

I would be surprised if there were not some anxious faces amongst the publishers as a result of PCORI's announcement. I also wonder, as I understand it, there are some journals, not to be named, which will not allow immediate access even if you pay $3,500 or whatever the publication fee is for immediate access to happen. They just don't have that option.

Effectively, it seems that would screen out

those journals for PCORI authors to be able to submit to, some of them might be journals they want to. I wondered if you have been hearing any noise about that.

DR. SELBY: I have not heard any. Unfortunately, Bill Silberg is not here. Yes?

DR. NORQUIST: Jean.

DR. SELBY: Jean.

MS. SLUTSKY: Francis, you have a great question. Bill Silberg has been negotiating with the journal publishers around this. So far, we haven't received any negative response from any journal publisher that they won't give immediate access for payment, to put it on the other side of the firewall.

Now, we are also trying to negotiate bulk rates. Our policy doesn't require any authors to go to any particular journal. That is really their own preference where they are going to go. We probably at some point will encounter some friction, but up until now, we have not.

I take that as a good sign, but knowing the

likelihood of us coming up with the hard walls will likely happen, but as you point out, there is a lot of movement towards this, and given the language in our authorizing legislation, we just felt it was the right thing to do.

DR. McNEIL: That was a great report, Joe. I have a couple of questions. The first one is --

DR. NORQUIST: Barbara, is it on this issue or are you on a particular issue?

DR. McNEIL: No.

DR. NORQUIST: Let's let Harlan speak.

DR. KROMHOLZ: I just want to respond because I have heard from some of the prominent influential journals. I think there is a concern on twofold. One is the mandate around the public access, but the other is the one-month disclosure of the abstract with the results, which I think is an interesting thing.

I just wanted to enforce what you said. I think there will be. I think it is a good opportunity for us really to surface this policy in a very visible way, to engender a fair amount of

discussion, get people out there talking about it.

It could be that PCORI will see change in the way people think about this. It is going to be a question, I think, for the grantees who when they applied didn't necessarily understand all of the constraints, even though the legislation is there, but there was some interpretation.

To me, this is a thing worthy of Board deliberation because it is going to be a big policy issue. I would just say at least in my hearing on the ground, there are some major rumblings about what this entails.

DR. SIGAL: I say tough to those journals, this is the right thing for patients and the public.

DR. SELBY: All of our comments are based on --

MS. SLUTSKY: The other thing I wanted to say to Francis' comment to what about the journals that don't have a mechanism for that, we do have a mechanism whereby the draft final research report or the final research report can be posted at exactly the same time.

Even if we had a situation like that, we will have a way to get the result into the public domain at the same time.

DR. SELBY: Good point. That's a great point. Even if there should be a journal that doesn't give open access, our final report will be there.

DR. McNEIL: I have a question, this follows on Harlan. Does this mean that a written abstract that is published online would likely present publication in the New England Journal?

DR. SELBY: No. We are told no.

DR. McNEIL: I think it will. It definitely will, it's a historical basis to show that. There are miles and miles of data to show if you publish an abstract some place that is public, it precludes --

DR. SELBY: I was just told last week by one of the leading journals that the abstract is not --

DR. McNEIL: It is probably worth checking with Jeff Drazen in particular, because that is the

one that is the prickliest.

SPEAKER: Two years ago, Bill Orlando and I talked with the major journals, including the New England Journal, about our policy of abstract and publishing on ClinialTrials.gov, essentially immediately. They said fine, they didn't bother us.

They were bothered by the idea about publishing the whole article online, but the abstract, 500 words, they didn't have a problem with it.

DR. McNEIL: Would it be worth -- not to be too Type A here, I do have another question, but would it be worth confirming that for 2017?

DR. SELBY: Hopefully, we will get some chances.

DR. McNEIL: Here's the question I have, Joe. I actually have a couple of questions. The first one is I love the idea of evidence synthesis, but it strikes me that PCORI is doing it, AHRQ is doing it, and Blue Cross now has a very robust evidence streak approach.

DR. SELBY: Evelyn is going to talk in-

depth. I think first of all we are coordinating closely with AHRQ on this. Some evidence synthesis will actually be done through AHRQ, and Evelyn is going to have a whole discussion of this this afternoon.

DR. McNEIL: She will talk about evidence streaks?

My other question is the following. When you say "data sharing," do you mean patient level data on an item by item basis? Is that what you mean by "data sharing," or do you mean table one, table two, table three?

DR. SELBY: No, no. We mean sharing of the analytical datasets.

DR. McNEIL: The raw data or the aggregated data?

DR. SELBY: Raw data, not aggregated.

DR. McNEIL: Okay, that would be great.

DR. SELBY: Bob?

DR. ZWOLAK: Bob Zwolak, Board. I just want to congratulate everybody who was involved in the creation of this peer review process. It is

mandated by the law, but many of us thought it was a huge barrier, now we are looking straight at hundreds of manuscripts coming straight at us. I think based on the discussion we just heard, the entire Board will be anxious for regular updates.

DR. SELBY: Maybe even a Dashboard item or two. Okay, the Chair says to move on. Here is your third quarter. We are already past the fourth quarter of 2016. This is the third quarter report. Except for our new members, you know to sort of first look toward the yellow. Those are familiarly yellow. We are still a bit underspent in terms of the funds we have committed to research in 2016.

The top line, you will recall, is the maximum that we possibly could have committed if we had funded up to the maximum in every one of our announcements this year. The estimated is based on past experience that we get, usually fund about 75 percent of the maximum funds available. The middle bar is the estimated.

You will see that through the first three quarters, the first quarter is almost invisible, we

are on target. We are on target for what is expected, we are not on target for the maximum.

Over on the right, the expenditures. As in previous years, we are spending somewhat less on research awards, and my understanding is it is not more than 15 percent less, which is kind of a threshold for turning this yellow, but in terms of the non-research budget, these are budget expenditures, the left was committed, remember we have the old committed expended dichotomy, so under expenditures, internally, we are in fact significantly underspent, more than 15 percent, against the 2016 budget through three-quarters.

This is primarily due to having less staff on board at any point in time than we expected. That is due to mostly delays in hiring. We still had a number of people budgeted that had not been hired or were hired later than anticipated, as well as some turnover.

That is the main driver, in my understanding. Some savings figure in there, too. That is the main. We worked hard on the 2017 budget

to try to eliminate this chronic overestimation of expenditures.

We are not so worried about the research expenditures. We know they will catch up eventually. We are still a little bit surprised at how we tend to over budget in the other expenses.

Other things on here, you can see in the middle row, the left most box, we see the beginning of an uptick in the number of projects whose final progress reports have been submitted. That will really jump up in the fourth quarter.

I won't say anything more about these because they are green. I'm just going to go on to three stories. We always give you a couple of stories along with the quantitative, and I'm going to dive in this time as well to a particular issue on recruitment.

This is just a very nice publication of a network meta-analysis. You will hear more about network meta-analysis this afternoon from Evelyn. This is a study that proposed to do that work in meta-analysis and then build the results into a

decision tool and do a trial. This is the publication of the network meta-analysis in the area of treatment for Lupus Nephritis.

I am actually looking forward and anticipate that in the next year, we will see a publication of a number of systematic reviews in meta-analysis that were part of projects funded by PCORI.

This is as far as we can tell a spontaneous coming together of seven PIs, seven PCORI funded studies, all in kidney diseases, and they actually got together, began communicating, and wrote a paper together on the results of engagement, on the beneficial effects of engagement in research.

As far as we can tell, nobody from PCORI put these folks up to this, but three examples were written up. One was on how stakeholder advocacy led a major dialysis provider organization to find a new solution to accommodating novel treatment delivery options in order to participate in the study. Good news is the major dialysis provider organization flexed so they could participate in a study. That's

fabulous.

The second is a patient advisory panel, and another study provided feedback on the development of a decision aide, to help ensure it was appropriate for the target audience of pre-dialysis CKD patients and their caregivers, and the aim of this project ultimately is do a randomized trial of a decision aide, and the third is community engagement with the Zuni Pueblo in New Mexico, the process identified psychological and structural barriers that could be a challenge in a population with the world's highest prevalence of dialysis requiring kidney disease.

We are very excited that in the nephrology community and the kidney disease research community, there seems to be a network of patient-centered researchers that has gotten underway.

This was an issue on health affairs that PCORI helped to support that came out in April with a press conference that was third quarter. Six of the papers in this either had PCORI staffers and/or awardees, mostly awardees, it looks like, as lead

authors.

We had a press conference, and these speakers presented. It was a really remarkable and jam packed press conference. Those altimetric scores are all good, all reflecting that they are in the top five percent of research scored in terms of being accessed.

You have seen this before. I will just say this is the way in our post-interim progress reports that our program officers, engagement officers, evaluate projects ongoing. We have a lot of projects now that are ongoing. I won't go into the details. Green is good and red is really bad.

I want to say, too, that this is very hard work on the part of our project officers. I think in the beginning, there were a lot of doubts about whether it really meant something, but as we have continued to work, our evaluation people work with our science and engagement people. I think the confidence that this is meaningful has increased.

You will see starting from the bottom, which was a year ago, moving on up to the most

recent order, there is an increase, first of all, in the number of projects under review, not surprising. There is also a real absolute increase in the number and proportion that are in the green zone, it is modest, but it is definitely going in the right direction. More of the projects look to be on target in every way, including recruitment. There is always that small set of projects in the red.

The next slide here gives you a view of what happens to these projects over time. I like the news. If you take a look at those projects that were in the red or orange and follow them forward over time, you will see many of them come back to being -- in fact, two-thirds of them are either green or yellow. They have gotten out of the red and orange zone, a few stay in. Seven percent of the projects were terminated.

I want to say something about recruitment now. These are based on 211 studies that involve recruitment, so 211 randomized trials or other cohort studies, not surveys, and certainly not methods projects.

So, recruitment is on target or early in just over half, in 52 percent of these projects, as of their most recent interval progress report, and then 48 percent are either late or some of them have not launched recruitment yet. You will see that here in the dark blue.

The median is right on time, 59, but in the dark blue, that is late. You will see that most of the lateness is relatively short, three to four months or less. Then you see the distribution of the early ones as well. Just a few stragglers.

This just shows that if you were early or on time, you tend to stay in the same timeliness category, 63 percent, if they were early to start, they were early to finish. If they were late to start, they were late to finish. Of those that started late, actually 44 percent wound up ending on time. Of those that started early, 31 percent. There is some changing.

I think the good news is that overall, well over half of the projects that have been completed, 62 projects, have finished on time.

This is a report from Baylor that did the CME on our methodology standards, just with some very good 12-month data on responses from those who have taken the CME indicating that they intend to implement the methodology practice changes and engage patients throughout the research process in the coming years.

The knowledge also was believed to have been increased substantially, there at the bottom, of how CER contributes to advancements in patient care.

This is from PCORnet. This is really extraordinary news. Six months ago, on the left, you will see that there were almost no -- really a total of between 80 and 90 data marks, I think, now, and back in March, almost none of them were research ready.

They didn't have their data in a common data model, it hadn't been vetted by the coordinating center, and we have now gotten up to the point where well over half of our data marks are research ready, and in fact, have had queries run.

You will hear more about that in a little bit. Rachael Fleurence and Adrian Hernandez, the PI of the Coordinating Center, will be here to talk about PCORnet governance.

This is another piece of very interesting news from PCORnet. We just reviewed the letters of intent from Cycle 3 in 2016 that went out in August. Only a fifth of the about 400 LOIs that we received have mention or involvement of PCORnet.

It's a sign that PCORnet researchers themselves and others are beginning to think of and use PCORnet. Twenty-one percent of the broad's and 22 percent of the targeted pragmatic's and dissemination and implementation proposals involve PCORnet sites in one way or another. I think that bodes well for the future, for the sustainability of PCORnet, and for its use by the PCOR community.

That is the Dashboard, and open for questions.

DR. NORQUIST: Sharon? Then Ellen.

DR. LEVINE: Joe, just checking, the arrangement around free access to the articles, that

applies to [inaudible.].

DR. SELBY: No.

DR. LEVINE: [Inaudible.] The questions that are being asked are not good or people are not interested for all sorts of different reasons. What are we doing to make sure we have these controls in place to see early on what a problem is?

DR. SELBY: Well, I mean the first thing is we are monitoring very closely, so just to have this data is a good point. Our chief science officer.

DR. WHITLOCK: So, there are a couple things we are doing, Ellen. Because of knowing that this was one area where we were having challenges and it's always challenging for clinical trials, we are much more robust in asking about the feasibility of the recruitment plan in the applications.

We have beefed that up. We are focusing on that more during the merit review because we need to see that the plan is feasible in the first place.

The second thing we are doing is we are closely monitoring, and when things go off, we step up the monitoring. The third thing is we are

looking at the reasons. In some of these cases, the reasons are multi-site trials where something happens, they merge, there is a change in administration. It's the downside of pragmatic research, that you are out there in the real world where you don't have a lot of control.

We are trying to learn from those situations. We bring those to a troubled projects meeting and try to enhance the understanding across project officers and programs so that we can recognize those and support the researchers to get back on track.

I think the good news is many of them if not most of them are getting back on track. We are trying to work upstream to make sure we don't get into a problem in the first place.

DR. LEVINE: [Inaudible.]

DR. WHITLOCK: We do, and we are often having almost -- especially for things we think might be risky of people making their goals, we can have a stop point at one year if they really can't demonstrate, and we are doing that more.

Of course, once we have put the money in and it's a meritorious project, we're going to try to work with them, particularly when they have had structural reasons that are really not their fault.

Another reason is often IRBs. IRBs can take a year, and people try to get ahead of that, but it is a problem.

Those are all the things, and we try to not penalize people for things that are beyond their control, but also hold them accountable.

SPEAKER: Given this conversation, the data presented, I'll just raise an issue that I think I raised before, whether it is appropriate to put a green label on tracking research projects when we all agreed around this table this is an area that needs intense attention, and yet on the Dashboard, it still keeps the green label for research projects on track.

I think it is appropriate for us to be disclosing that this is an area that we watch very closely, and frankly, we are not entirely happy with the current situation, but we are working hard to

make it better.

DR. NORQUIST: That's a good point.

DR. SELBY: This is discussed a lot in the materials, too. Finding a benchmark is tough. I think even our conversations with NIH led us a bit away from making it yellow, just because they said this compares well with their experience.

I take your point, and I think with the Board's direction, would be happy to make this yellow and really continue to address it.

SPEAKER: I think that serves us well to set a very high bar for what we expect.

DR. NORQUIST: Leah?

MS. HOLE-MARSHALL: Thank you very much and for the additional materials that were in our packet, especially on this topic, I really appreciate it. I really appreciated -- I had started to do some math, and then I got to two more PowerPoints and was oh, there it is.

My question really is around the orange and red, because that is the reason to call attention to it, as opportunities to improve. I appreciated

Evelyn's comments. We still have 25 percent of projects that have been in red over a year. Is there a way where we can start to mature that criteria where maybe we have some criteria around -- it might be reasons.

I heard Evelyn mention there are some reasons that we still feel comfortable even though it has been more than 12 months in red and remaining in red, that we are willing to continue the progress, or maybe there really are some stop lines and criteria to consider. I think we need to continue to be thinking about that.

Overall, three of the projects were terminated in terms of total numbers, even though over 30 have been in red or orange for over a year.

DR. SELBY: Excellent point, and a nice job of pulling facts out of data. I will say we continue working very hard on these. It is a lengthy process to terminate a study and we don't put it up here unless it really is terminated. I think you will continue to see an increase in those numbers.

MS. HOLE-MARSHALL: Again, I'm not advocating for premature, it takes a lot to get there, but sometimes I feel like the hardest thing is knowing when to stop something. If we had some continuing either focus or criteria that we start to develop and that we can let our awardees know, here are some things that really for us mean no go.

DR. WHITLOCK: I can report back on that. I can report back on a qualitative assessment. I will reassure you that the troubled projects consortium contains legal input and contains all of the program directors, so we are looking at this carefully. I think we can report back so you have a sense of that.

I also want to reassure you that there is a time between decision making and contract award, and if things go awry at that point, we are working with Legal to make sure we don't award things that we already know are not going to be able to be feasible. We're trying to be diligent throughout the process.

DR. NORQUIST: Great.

SPEAKER: [Inaudible.]

DR. WHITLOCK: To the first question, one example of that, and as you saw from Joe's presentation, many people are coming in now citing PCORnet. One place we went awry was there was a citation of PCORnet without actually getting the agreement that all the sites could work and therefore, the feasibility was not there.

One of the things that we are building in is some understanding of how PCORnet is being cited and is there evidence that the coordinating center and/or the clinical sites themselves or the PPRNs have agreed, so letters of support, I think, is a really important area for feasibility.

In terms of the modification, on the Selection Committee yesterday, they just made a series of decisions about what can be modified between merit review and award, and bringing it to the Board, I should say, post-award. We might be able to come back through our contract data. I'd be happy to report that out.

DR. NORQUIST: Okay. Francis?

DR. COLLINS: I think the publications are gratifying coming out of PCORI funding, but I think the critics and the stakeholders are going to be particularly interested in publications that involve primary data, A versus B, which obviously have a longer lead time.

The examples you showed were interesting but they were not of that sort. I would be interested at least as one Board member in having some separate accounting of how are the publications looking at far as those CER primary studies, because I do think that is what a lot of people are waiting for and watching, and we ought to be able to quickly track that and not have them buried beneath a whole pile of other kinds of articles.

DR. SELBY: That is an excellent suggestion for an improvement to the Dashboard, and we can incorporate it for the fourth quarter.

We just got a note to remind everybody to please speak directly into your microphone. There is something about these mikes that is not picking up well. Even though it sounds like they are

amplifying, people on the phone are not hearing.

DR. NORQUIST: That is what we are hearing.

DR. SELBY: I am really pleased to introduce a person you know well, Rachael Fleurence, and Dr. Adrian Hernandez from Duke University and Duke Clinical Research Institute, who is the principal investigator of the Coordinating Center for PCORnet.

This presentation is entitled “PCORnet Governance.” It arose out of a question that a couple of Board members asked about where is PCORnet really going. We told them a little over a year ago now that they need to start planning for their own future for sustainability.

One thing that could happen is PCORnet could cease to have funds after September 30, 2019. The Executive Committee launched a really robust sustainability planning process, but this raised questions about the patient-centered perspective, and are a broad set of funders going to remain part of PCORnet’s vision.

Rachael and Adrian are going to address

that. Thanks very much for being here.

DR. NORQUIST: Let me just ask a question, Rachael, I know it is like three different sections. Do you want to hold discussion until the end of all three or do you want to interrupt and have discussion as you go?

DR. FLEURENCE: We should probably wait until the end of the formal presentation.

DR. NORQUIST: I would ask that the Board members, if you have questions, just write them down. Let's let them get through their presentation. Thanks.

DR. FLEURENCE: Thank you and good morning, everyone. I am pleased to come here this morning, as Joe said, to talk about the current and future planning around PCORnet.

My part of the presentation is talking about how we are keeping PCORnet's mission aligned with that of PCORI, so you are going to hear what we are currently doing to put these safeguards in place. Adrian is going to talk about the actual plans for moving PCORnet into its own independent

entity.

I'll talk a little bit with a very brief reminder of the achievements to date, and then we will go into the planning. I'll talk about governance and Adrian will talk about sustainability.

This is a very quick reminder on this slide of where we have been and where we are today. PCORnet launched in 2014, January 2014, with 11 clinical data research networks and 18 PPRNs, and a coordinating center. In October 2015, phase two of PCORnet began with 13 CDRNs and 20 PPRNs, and a Coordinating Center.

Just as a reminder, many of you will remember that PCORnet was born out of a vision of the Board in 2012 after a large multi-stakeholder meeting, and was really created to address gaps in the U.S. national research infrastructure.

A very brief summary of achievements to date. PCORnet has been up and running, coming up to the end of its third full year. Just a reminder that it really went from a blank page and a vision

of people in this room to involve participants in all phases of research and to use electronic health data to conduct rapid comparative effectiveness research.

Phase one of PCORnet was focused on really building the network with a focus on governance, on developing the individual PPRNs and CDRNs, and laying out the vision and plans for a common data infrastructure for distributed research.

In phase two, we continue to build these building blocks, developing individual and PCORnet-wide sustainability plans, continuing to focus on administrative simplicity, that is streamlining contracting and IRBs, which really do continue to slow down research being conducted.

We continue to implement the distributed research network for both observational studies and pragmatic randomized trials. We have a number of demonstration projects that have launched this year and they are currently underway.

Planning for PCORnet's future has been at the forefront since the beginning of this

initiative, and it was actually the Board's intention back in 2013 for PCORnet to become a sustainable network after PCORI's initial investment. This has always been part of our work and our planning. This little abstract here is simply what was in our phase two funding announcements. The requirement that each individual network be planning for their own sustainability as well as sustainability of PCORnet as a whole.

Current planning for the future is well underway on two fronts. First, the governance model that ensures that PCORnet stays mission aligned, and second, a sustainability model that supports PCORnet's continuation after PCORI's initial investment into PCORnet.

I'm going to talk a little bit more about today's governance and how we are maintaining and putting in place safeguards to ensure PCORnet's mission is aligned with that of PCORI.

PCORnet's mission is to enable people to make informed health care decisions by efficiently conducting clinical research relevant to their

needs. This mission statement has been developed over the months with input from hundreds of folks within the PCORnet community, clinicians, investigators, as well as PCORI staff.

This is PCORnet's current governance structure, and it really reflects that PCORnet is still very much a funded entity, an entity funded by PCORI with 33 contracts that belong to PCORI and that are monitored in the way PCORI monitors contracts.

You will recognize here sort of a fairly traditional governance structure with 33 investigators or patients sitting on the PCORnet Council, formerly a steering committee. There is an executive committee that has representation from CDRNs and PPRNs.

We have three critical committees that really are taking care of data engagement and research strategies within PCORnet, and we have a coordinating center. All of the committees include patient representation and keep the mission of PCORnet at the forefront of their minds as they

execute the strategy.

A few points about how the governance supports and protects PCORnet's mission. Here are some safeguards that are in place in the policies to preserve PCORI values and ensure mission alignments.

First, the governance policies that are adopted by vote by the PCORnet Council. They require that patients be on each of the committees that run PCORnet. The governance policies require that any PCORnet designated study be patient-centered and include patient engagement, and these requirements are reviewed by the PCORnet committee members which also includes patients.

The networks themselves within PCORnet are required to have engagement policies and procedures as well as patient leadership on their own individual governance structures.

Any policy amendment within PCORnet has to be approved by a simple majority of both PPRNs and CDRNs, and all policies are currently subject to final PCORI approval, PCORI staff does have sort of a veto right on any PCORnet policy which we have not

had to exercise to date. As we plan for the future and we look into PCORnet future governance models, several safeguards are being discussed currently to ensure there is continued mission alignment after PCORI's initial investment ends.

It is likely there will be a governing board for PCORnet. Its role will be to ensure that there is mission alignment. PCORnet sort of in blunt words will not become a CRO, it will really ensure any project conducted within it is aligned with its mission.

There have also been discussions of hiring an ombudsperson that would be dedicated to providing objective oversight on the policies and activities of PCORnet. The role of future funders of PCORnet research is currently being discussed and determining the optimal breakdown between the sources of funding, and it also is a matter of discussion currently.

I just have two more slides to talk about how we see PCORnet evolving in the future. One is the intent right now is to have a mix of both

industry or private funding as well as public funding from a number of non-governmental agencies. One key development in PCORnet is what we are calling "collaborative research groups."

These are opportunities for researchers and stakeholders to engage in specific areas, generally these areas, but not always, that align with Federal research priorities. You can think of CRGs as sort of clusters of investigators, patients, clinicians, advancing research in these particular areas. There are some examples there on the slide where we are going to be considering CRGs in cancer and pediatrics, cardiovascular health, health disparities, et cetera, and a few more.

You can think of these as sort of small almost business development units that will be working with NIH and industry to increase the volume of research within PCORnet.

My final slide is a slide that was actually developed by our colleagues at the FDA, and it looks at PCORnet in a bigger picture at the national evidence generation infrastructure.

You will see PCORnet is right there in the middle of this so-called nexus, but the PCORnet GHR data linked with claims data is part and parcel of this national evidence generation infrastructure that will support more rapid evidence generation for many stakeholders within the country.

With that, I'm going to hand it over to Adrian who is going to talk to you more about PCORnet and sustainability.

DR. HERNANDEZ: Thanks, Rachael, and thanks for having me join the meeting here. As Rachael noted, there has been a lot of work done for PCORnet, and also thinking about how PCORnet can be sustainable, and ensuring it is also maintaining its mission as it develops in the vision of 2012.

Currently, the sustainability approach is actually multi-fold. One is we want to continue to build on infrastructure and assets that have already been developed for PCORnet, so that investments that PCORI has made into PCORnet for developing the common data model, linking electronic health records across 100 or more health systems across the U.S.

into a common platform.

Further and continuing the infrastructure development that has already taken place, using that with other data sources, including insurance claims and patient reported data as well.

As part of building blocks, PCORnet has built on research partnerships that have developed across CDRN and PTRN partners, and also really using novel and pragmatic approaches for doing a study. This includes engagement at the beginning and throughout the conduct of studies, empowering people in communities for developing the questions, ideas, and approaches to answering questions, using novel methods for doing clinical trials that have not yet been done at scale, such as e-identification, e-randomization, electronic consent, using a single IRB to facilitate the conduct of research.

We have already begun proof of concept across PCORnet in observational studies, as well as pragmatic trials have developed proof of concept that yes, this can be done as part of this.

We are releasing information regarding who

is in PCORnet, such as demographics and conditions of people in PCORnet, providing updates on both the observational studies as well as the pragmatic trial development, and also opening up the PCORnet front door for interested investigators and partners for using PCORnet.

Further, we have also done a landscape analysis to understand what else is out there, and how PCORnet can uniquely fit a niche that has not been met today in terms of doing clinical research, and making sure we fit into a space that is currently not occupied and that can further enhance the mission as well as be able to deliver clinical research that matters.

This does require building relationships and partnerships throughout the U.S. and across the different network partners in PCORnet, and then also developing a plan to create an independent entity to ensure sustainability and administering simplicity as well as enhancing ongoing efficiencies for PCORnet.

The operational model is shown here at a

high level. What the current plans are is PCORnet needs to be functional for multiple partners in terms of funders as well as those who actually are doing research.

If you think about the research market, PCORnet is well-suited for doing government agency sponsored research, PCORI sponsored research, as well as industry and non-profits who have interests that align with PCORnet's mission.

An independent PCORnet entity will be formed to allow administrative simplicity for these funders to access and join PCORnet for conducting research. This independent entity can also facilitate innovations for PCORnet, as well as allow easy joining of PCORnet by the various network partners.

A virtual coordinating center would provide services and a lean approach for research program development, as well as using the tools of PCORnet and growing the tools and suite of activities for conducting PCORnet research, and through all this, the CDRNs and PPRNs would be part of the PCORnet

operations.

Just to give some highlights regarding what we have seen for the research market, we have been doing a number of interviews across various funders as well as partners for research, including those here in this room as well as other outside funders.

We are already seeing a large interest in the PCORI community with over 20 percent of LOIs proposing to leverage PCORnet resources. We also are seeing a PCORI funded trial, COMBINE, which is a collaboration of CDRNs and PPRNs coming together, and also we have in development Federal funded projects that are co-partnered with FDA as well as the CDC and NIH.

In particular, leveraging PCORnet as a partnership with NIH, bringing together CDRNs as well as TTSAs and other groups for doing highly pragmatic high impact clinical trials, such as INVESTED, which is evaluating influenza vaccine on cardiovascular and pulmonary outcomes.

Regarding industry engagement, just like this room represents, we realize the research market

has a lot of different interested parties, and especially those who are interested in the mission alignment that PCORnet has put forward.

Specifically, their interest in terms of understanding and being able to improve people-centered or patient-centered outcomes, and through this mechanism, we have developed an industry work group that was originally providing information back in March 2015, and also gaining an understanding of what their interests and needs are, as well as where PCORnet could fit or not fit with those aims.

These discussions have continued, and we had reconvened a smaller group of early adopters of PCORnet this summer, and then we conducted a series of one-on-one interviews as well as teleconferences, culminating with a meeting last week of different industry partners, to understand what are the resources that we have available that would be of mutual interest, as well as understand how we can have an operating model to do PCORnet research.

This has generated a lot of interest, and actually interesting developing pilot projects

similar to what PCORI has funded so far, in terms of demonstrating in a multi-stakeholder patient-centered orientation of improving the value proposition of PCORnet, and also understanding how PCORnet can be used for both observational studies as well as pragmatic trials.

These are the companies that have been part of this early working group, and when we showed them just the topics on the CRGs across these organizations as well as the specific disease topics and broader topics, such as health disparities, all of them have genuine and high interest in all those areas.

What has come out from this industry work group is actually developing and getting a refinement on what we view as different products and services in the three categories of data, engagement, and research.

They have also provided input in terms of how they are able to engage in PCORnet funded research and providing input in terms of what the operating model and business model could be for a

PCORnet future entity.

We also explained to them how PCORnet is organized currently in terms of governance and partnership, and how that would need to be organized in a future entity. They were very supportive of that because this is a unique ability for doing research differently that hasn't been done before.

Moving forward, we are working to develop a collaborative project that would be in a pre-competitive space, that can be multi-stakeholder and multi-sponsor project areas, such as key research queries and different conditions, such as diabetes and cardiovascular health, early observational studies on described populations, treatment patterns and conditions, are of great interest.

Doing simulated studies to further understand the quality and methodologic issues regarding PCORnet data, and also doing comparative studies to see what has been done traditionally with industry versus what is possible in a unique PCORnet model.

This has all come together under a larger

umbrella towards real world evidence generation, especially of interest currently as the FDA moves forward with PDUFA VI and MDUFA, and their entrance into real world evidence generation, and we feel with PCORnet, we are well positioned to address many of the needs that have been outlined in PDUFA VI and MDUFA.

Let me stop there and answer questions.

DR. NORQUIST: Gail, I think you had your card up long ago, and then Francis, Larry, Ellen, Alicia, and Bob. Gail first.

MS. HUNT: I just wanted to say something to Rachael, and that is that I would really appreciate it if you would include family caregivers in some of your discussion about how important it is to involve patients. In many instances, family caregivers are really the critical link to adherence and all that.

DR. FLEURENCE: Point well taken, and we do have patient-powered research networks that are particularly focused on caregivers. We had an Alzheimer's PPRN particularly. I apologize for that

oversight.

MS. HUNT: Do we have some family caregivers on the PPRN oversight coordinating committee?

DR. FLEURENCE: I believe we do, both from the autism and Alzheimer's networks.

DR. NORQUIST: Francis?

DR. COLLINS: I appreciate the update and like the way in which you are setting this up, including having a front door. Sort of sounds like you're setting up an Airbnb. With Airbnb's, it is all about what is the track record, had the previous guests had a good time, were they well taken care of, was the furniture all right, was the breakfast nicely put together.

I suspect as you are talking to industry and other potential clients of the PCORnet, their most pressing question is, is it working, have there been now some successful experiences of other guests who have come to your Airbnb and have gotten great data out of it.

I guess it would be very helpful if you

could quickly summarize, where are we in terms of seeing the first big results coming out of PCORnet with the studies that PCORI has been funding, for instance, with aspirin?

I think the emergence of those data is going to be critical for people's interest in walking through your front door.

DR. FLEURENCE: Thank you for the question. We currently have three major research/demonstration projects underway, the observational studies and the one pragmatic trial which is what you referred to. We have a number of other research demonstration projects in the pipeline, and I may talk about that a little bit afterwards.

It is important to remember that these are both research and demonstration projects, so they were funded to not only provide -- whet the appetite of future funders, but also funded to help build the infrastructure in a focused way. In that sense, there are learnings that are happening along the way with these first three big studies.

The observational studies actually have

been absolutely instrumental in finishing building out the distributed research network. They have allowed us to have 117 data sharing agreements signed across the country. They have allowed us to do the data characterization across 80 plus data marks, 60 of which are now approved for research.

The two observational studies are well underway. They are overpowered for the aims of the study. We have about 30,000 patients in the bariatric surgery sample, and we have 350,000 patients in the antibiotic study. These will be the largest observational studies of their kind in these particular topics.

While they have taken a little longer as observational studies than the regular observational studies, I hope I have made the point that they have really helped us build out the infrastructure this year, and they should be reporting out on their aims in the first and second quarters of 2017.

DR. NORQUIST: I guess the question is, it sounds like the guests are still there. Do you have a rating yet, I guess, is the question? What would

you say? You built it up. The question is at this point do we have a trip advisor rating or whatever?

DR. FLEURENCE: If you don't mind, I'll just finish my little description on the pragmatic clinical trial, which is our other big built out for the PCORnet infrastructure, and then I'll go to your question, is there proof of concept or is there interest or were the guests happy with the food.

On the pragmatic trial side, there have been some delays in actually activating and launching with contract signing and IRB issues. These delays have actually been due to the difficulty in convincing IRBs of the use of novel methods to identify and consent patients outside of how clinical trials are normally conducted.

We have seen sort of an expected, I think, delay in launching. We have now launched, and the proof of concept, I think, we are starting to see is there. A large number of patients have been identified through electronic records. They are being consented in various ways. This is very different from traditional pragmatic clinical

trials. They are being randomized electronically after a quiz, in order to make sure they understand what they are consenting to, and then we are implementing all these methods for electronic follow up.

Really, decreasing the burden on clinicians and actual patients themselves in participating in this trial. To date, there are over 400 patients recruited and 35 percent of these patients were recruited in the last month. We have a number of sites activating in the next month, more sites activating in the next month.

That is sort of just a brief description of where we are at with the observational studies and our pragmatic trials.

To your question, Francis, are the investigators happy and is sort of the future funding community happy. I think there is certainly huge interest in the novel approaches that have been developed to scale with what PCORnet can do, the diversity of the institutions that are included in these studies, both on the observational side and on

the pragmatic side.

Sort of the third piece is great interest particularly to the industry funders, our ability to work very closely and really co-produce the research with patients.

I think my answer would be everything is well underway right now in order to obtain the proof of concept for PCORnet and the scale of what we have developed in the last three years, and the conversations are underway with the funders.

No one yet has given us a rating of they're not going back.

DR. COLLINS: Do you have an estimate of when publications would appear from the observational studies and the pragmatic trial?

DR. FLEURENCE: That's a good question. I imagine some time in the third quarter of 2017 for the observational studies. The pragmatic trial is longer, it is a three year trial. It's going to be a little longer.

This week, we are publishing our first data on what we are calling our current demographic and

conditions, that should be going out this week. We are also starting to sort of trying to publicize more where we are at and what we have done.

DR. HERNANDEZ: Let me just add a couple of comments as well. In particular for pragmatic trials, we are breaking through institutional and cultural barriers. There are a lot of gatekeepers in terms of being able to contact potential participants at a large scale, being able to actually use the electronic consent platforms, and even including the questions there.

Those are barriers that are now being broken through that can be reused or pathways for other future pragmatic trials to be done. Based on just even our adaptable study meeting that brought investigators, patients, and the community together on Friday, we actually outlined over 10 different perspectives and areas that we were going to put out there in the public domain on lessons learned already to outline these different issues that everyone else will need to actually rally behind for that change. We will put that out there.

While our outcome in terms of adaptable will wait until the completion of the trial, along the way, we are going to publish in a variety of forums, including lay as well as traditional press, publications, and journals, what are the lessons and what have been solutions, and then what are future barriers to overcome.

One of the things I'll just noted based on our Friday meeting, we actually made a commitment to the adaptable research community that we are actually going to inform the participants first of the results, before traditional publications.

The results will go to the participants first, and then we will see if a journal is ready to publish it after the participants here.

DR. NORQUIST: Larry, and then Ellen.

MR. BECKER: Could you take a moment or two and talk about your process for conflicts of interest, real or perceived, and the independence of the research?

DR. FLEURENCE: The conflict of interest for? Which part?

MR. BECKER: You are taking in money from various places, and conflicts arise, conflicts of interest. What is your process to make sure the research is independent and not influenced by funders?

DR. FLEURENCE: Okay. PCORnet as a sort of legal entity does not exist to date, so technically, PCORnet itself has not taken in any additional research funding. The demonstration projects I discussed are PCORI funded projects, and therefore, they are under the PCORI conflict of interest and processes.

In the future as PCORnet becomes its own entity, there will absolutely have to be robust processes in place in order to determine criteria for undertaking and conducting the research.

Currently, the PCORnet research committee has developed sort of some initial criteria around that, but I do think it is a process that is underway but not yet fully relevant since the PCORnet studies are currently mostly PCORI funded or NIH funded, or co-funded with FDA.

DR. NORQUIST: Ellen?

DR. SIGAL: Rachael, I have a few questions, and some of this gets back to my experience. One is what is the overall cost for infrastructure, what is our basic cost? I have two or three others that are aligned with that.

DR. FLEURENCE: The current figures, and I'll be discussing them in more depth tomorrow at the joint SSC/RTC meeting, so the current figures are, total funding including research, about $330 million over the two phases, and about $280 million, I believe, for the infrastructure funding alone over phase one and phase two.

This includes infrastructure funding for the 13 CDRNs, the 20 PPRNs, and the coordinating center.

DR. SIGAL: The $280 million is costs going forward for how long?

DR. FLEURENCE: The $280 million is the full cost until 2019.

DR. SIGAL: What I'm interested in is the sustainability moving forward. Is it $50 million

just for infrastructure, all those things, and for this to be sustained beyond, we need to understand that.

DR. FLEURENCE: The way I think about this is there has been a major initial investment by PCORI in building this infrastructure. The marginal cost of sustaining PCORnet will be slower because of this additional investment into the building blocks.

These are critical questions around sustainability, and they involve individual CDRN networks and PPRN networks being able to maintain some sustainability individually, and then PCORnet as a whole being able to maintain its own sustainability.

The costs of actually maintaining a future PCORnet are actually smaller than the $280 million that I described, there will be a central program office whose role will be to do business development, maintain standards, and maintain a very kind of lean program office. Other work will be conducted at the individual CDRNs and PPRNs who will maintain the current data infrastructure through

research projects that are going to come through PCORnet.

DR. SIGAL: Maybe I can sit down with you later on and talk about this. The one thing I will tell you is there was sustainability after putting in the hundreds of millions of dollars in central, but the methodology, which was funded initially at the NIH, now at the FDA Foundation, has been very difficult now as we go to a user model.

We are finding few people if any want to pay for methodology and for research going on. That is something perhaps we can talk about.

Of course, obviously, your diversity of funders and conflicts of interest. Really, you should have a better grasp on exactly what the infrastructure cost is going forward and who is going to pay for that, and of course, questions will come from different sources. It's not easy, and again, continuing the research component and who pays for that and methodology, that is another whole issue.

DR. FLEURENCE: I agree. These are all the

key questions we have to grapple with, and it is not an easy challenge.

DR. NORQUIST: Alicia, we will let you go, because you seem very anxious. Then we will let Bob go.

DR. FERNANDEZ: I don't mean to be anxious. I hope I don't come across as anxious.

[Laughter.]

DR. FERNANDEZ: I think John is anxious about my comments.

[Laughter.]

DR. FERNANDEZ: I want to start by thanking Rachael and Adrian, whom I know, we did residency together, for outstanding work in terms of going from zero to what we have now.

However, I want to take us back to slide 41, and I want to talk to the Board, and also have the two of you weigh in. We have invested or will have invested $610 million, roughly, if I added correctly, 330 plus 280, of public monies into PCORnet. As Harlan has told us, we will likely be judged, PCORI's success will partly depend on how

PCORnet does and moves forward.

I think to extend Dr. Collins' metaphor, what I want to focus on now is who owns the property. It would be great if it gets good ratings, fabulous. We need it to get good ratings. We need it to be useful. Who owns it?

As it moves forward and the real estate market changes, and travel gets disrupted in other ways, who will make sure it stays valuable, that it serves the community it needs to serve, that it maneuvers its way through changing landscape?

I think that is a discussion we need to have now, and I have spoken at length with both of you, and you have been extraordinarily receptive.

I want to put forth as a proposition that a governance model constructed of researchers and patients is insufficient and PCORI needs to resolve that now before we construct another legal entity, and we need to figure that out, what happens if PCORI sunsets, what happens if it doesn't sunset? How will PCORnet go forward?

I think I circulated among the Board

members, and apologies if I missed the two newest Board members, a very interesting and important article that came out in the Annals two weeks ago, showing the relationship of patient groups to the FDA process.

What that article indicated was that patient groups play a very valuable role in the FDA, but a good 20 percent of them are also sponsored by industry and continue to maintain industry roles. Regardless, even if we can all agree on the definition of what is a patient group, which I don't think we should try to attempt, there are more stakeholders, as seen around this room, than patients and researchers.

Where are clinicians? Where are other people who will continue to make sure that this wonderful property stays for the people who invested in it, which is ultimately the public at large.

In this slide, you outlined some of the things that we are thinking about. Will we think it is okay for the PCORnet breakdown to be 90 percent industry/10 percent NIH? Maybe that is okay.

I would say maybe not, but would we ask for you simultaneously to become sustainable, and as Ellen points out, that's not an easy thing, and yet we don't ensure a governance model. I think it is easy to see the conflicts and the pressures that will be brought to bear on PCORnet.

I will stop soon. My comment to the Board is we don't have a committee that's organized to look at PCORnet's governance. Is that the RTC? Is that the SOC? Who is doing it? We have had no spirited debate on who are the owners of this wonderful new building, and I think we need to do that. Today, our five minutes are going to be up soon.

I don't think we should leave today without at least some focused discussion on this central question, which is a question of governance. Who is going to resolve it? How is the Board going to be involved? How will we interact with Adrian and his colleagues around all of that?

Thank you all.

DR. NORQUIST: Freda, I think since you are

the chair of the RTC, I think this is something to which you should respond.

DR. LEWIS-HALL: The RTC has been paying attention to this issue as kind of the committee that oversees the evolution. We have recently combined the RTC and SOC to begin to ask some of the critical questions that you have asked about, you know, if this is the infrastructure, then who is really overseeing the entirety of the work that happens moving forward from a research plus infrastructure standpoint.

We had our first joint meeting, and have plans for moving forward. Those are really the two committees right now that are focused on this. Our plan is to continue to evolve the governance platform and bring it back to the Board as a proposal, if you would, for full discussion.

I took notes while you were making your comments, because I think three things. Thing number one is maybe we will move up the discussions and plan more than one, a series.

Two is our plan to take a look at some of

these governing principles, but I'll make sure that we add in this kind of conflict or potential conflict that you see, and the idea that one of the potential resolutions for that or mitigating against that would be to have a governance board that is constructed differently than perhaps what we may considered thus far.

More often to the Board, an ongoing conversation, continue the RTC and SOC discussions as they have been, and then to put an exclamation point behind your questions about whether or not we can do a better job of managing the potential issues moving forward by changing some of the conversations we are having about governance.

DR. FERNANDEZ: Thank you so much, Freda. That sounds wonderful. The only thing I would point out is we probably have some process underway to spin off the PCORnet entity, and the governance part should be in place before obviously that happens. Once it becomes a spin off, it's spun off.

DR. NORQUIST: I think that is what Freda was saying.

DR. LEWIS-HALL: Yes. I also want to add that I think the evidence generation platform slide was a really critical one, because it really suggests that the conversations we have been having alone as PCORnet are now going to be in a different context because however these things move forward, we are now going to need to consider how and if it would operate more productively in the context of a national evidence generation platform.

What happens if the PMI is onto that? What happens if the NIH collaborator -- how do we look different as kind of an engaged national platform? We have that additional insight to bear on this as well.

DR. NORQUIST: Alicia, nothing should preclude you from having ongoing discussions with Freda and the others about what concerns you may have. I would encourage you to have ongoing kind of discussions. Bob?

SPEAKER: Thank you. My questions also follow about governance, and the issue I think in my eyes is focused on two slides. If you go to slide

39, which is sort of the current status with PCORI at the top, and I'd like to focus on the coordinating center, which is the dotted line off to the right, mostly a service function, I think.

If you go to slide 46, which is the plan, PCORnet operations, the coordinating center forms a gigantic block in the middle between the front door and the CDRNs and PPRNs. It seems to me that is a relatively dramatic change and uptick in the responsibility of the coordinating center.

In your thoughts about the independent PCORnet operation, is this slide 46 actually how you perceive the coordinating center, and then from a business model, what is the current burn rate of the coordinating center?

I assume almost all the money now for the coordinating center comes directly from PCORI, and yet in the new independent model, I would assume -- is the coordinating center the collector and then distributes money out to the CDRNs and PPRNs, or does it go in the opposite direction, that the CDRNs and PPRNs have projects and they fund the

coordinating center for administrative functions?

DR. HERNANDEZ: Let me address that. What this depicts is really a virtual coordinating center. For this to actually work at scale, we actually have to have coordinating center functions across PCORnet. Taking advantage of the different networks that they develop, centers of excellence, specialties, similar to what is being outlined for the different collaborative research groups.

The coordinating center function will depend on the various aspects of the network. Our aim was to actually create multiple coordinating centers for PCORnet, so there is a broad band for doing research.

The concept here specifically is there will be a set of common services that would need to be really lean, so in terms of projections of overall revenue, it would be in the range of 4 to 6 percent of total revenue, so aiming to keep it much smaller than what a typical coordinating center activity would be for an infrastructure, which usually for NIH trials or NIH networks, is on the order of 25 to

50 percent of total revenue.

The other thing you bring up in terms of the burn rate, and it ties to Ellen's question earlier, we do have a minimal cost model for the different networks as well as what the coordinating center functions would be. It depends on the total size of the network. You can imagine if there are say 100 different health systems and network organizations, the total cost can be quite large.

On average, in terms of a network or coordinating center function, it varies in terms of a few hundred thousand dollars to several hundred thousand dollars, so trying to keep things in terms of minimal costs or a burn rate that is needed for future activities at a low cost. Right now, it is all infrastructure building, but certainly we can't maintain a business model at that level of funding.

DR. NORQUIST: We have Barbara and Andy.

DR. McNEIL: Thank you. I have actually two questions, and one of them is amplification on what Alicia talked about. Assuming this moves on to an independent organization, I know, Rachael, at our

last meeting, you raised the issue of funding another $40 million towards this group, and I see it is in one of the slides for tomorrow.

I wondered if you could say a few words now about why that would be useful, and why it would be useful to use that now if we wanted to spin this organization off as an independent entity ultimately versus using additional funding of our core research work, and Evelyn told us yesterday at the SOC that we may have other money for some of our regular projects going forward, independent of PCORnet.

I wonder if you could say a word about that, and then I have one more question for Adrian.

DR. FLEURENCE: The question about the $40 million in the PCORnet budget moving forward, so 2017, 2018, and 2019, $20 million of these dollars were earmarked by the RTC in order to continue doing work with the patient-powered research networks to fully leverage the power of patients and communities in PCORnet, so really sort of take what we have now learned from the current PPRNs and move that to another level of engagement.

Currently, that money is divided into $10 million under research and $10 million under infrastructure. Whether that would be the final make-up of that bucket of money, I think, is to be determined, and any project would have to come in front of the RTC, the SSC, if it was under research, and then the full Board for approval.

This first $20 million was earmarked at the request of the RTC in order to really further leverage and develop the patient and community engagement within PCORnet.

DR. NORQUIST: I think we will go into more detail about that in the meeting. I just checked with Evelyn. We're not running out of money. We can clarify that. We don't want to give the impression that somehow we are running -- there is an issue that we will come to a point at which we have to make choices about where we are going and where we will spend our money, but we're not running out of money. I think it is where we leverage our money and where we put it at this point.

I don't want the perception that we are

running out of money at this point. It's where we put our money at this point. I think tomorrow we can have more of a discussion on that.

DR. FLEURENCE: I'd like to make just one final point because it goes to Alicia's point about sustainability. To put it bluntly, PCORnet on one extreme could become a CRO doing industry funded projects, or on the other extreme, could be looked at as a public good thing, purely publicly funded research.

A public good needs some continued investment for the infrastructure, there is a cost involved in maintaining the data infrastructure that we have developed. Whether it needs to be as large as we have, I think that is a question for the Board to look at, whether we do need 117 institutions across the country, whether all data is of equal quality. I think these are important strategic questions for the Board.

The second $20 million that you discussed, Barbara, are money that is potentially earmarked for the ability for PCORnet to be able to launch into

its new status and be able to maintain some of that data infrastructure that would be needed to continue funding those public good type projects.

DR. McNEIL: I think it would be great to have really detailed data on both of those components. I do have one question for Adrian. I think we talked about this before.

You mentioned the use of the data mark, the common dataset and how that is being widely expanded and used by others. The question is there are many other common datasets around, some of which for various kinds of clinical studies.

Here's the question. To what extent do you think your dataset or your common data model will take over the world and will become the one that everybody uses? If it isn't, then you might -- talk to me about the pro's and con's.

DR. HERNANDEZ: Sure. We describe PCORnet as more than data, data is necessary but not sufficient, so one of the key components, and we hear this from multiple stakeholders, being able to use the data in new ways which incorporates new data

streams in terms of what is actually available in the health systems, but also data streams that are directly derived from people.

The other thing is actually being able to engage large communities at large in a more rapid fashion than what has been done before, so then it allows those communities to say yes, this data can be used for this purpose.

A third thing is actually getting back information to people. When we do a study, if you actually can imagine, say for adaptable, we have hundreds of thousands of people that have actually been identified. We can report the results rapidly to the 20,000 participants but then we can also report back the results to all the others that are adaptable like patients.

The common data model is a core asset, but a key component is actually what are other modules in terms of data assets that are added to it, as well as the engagement parts of it, and the pre as well as the dissemination sites.

DR. NORQUIST: We are way over here. Andy

and Bob. We are going to have much more of a discussion about this tomorrow. There have been some wonderful comments. Adrian and Rachael, we thank you very much for this. There will obviously be some things to bring back to the full Board here at some point.

Andy, and then Bob, and then that will be it.

DR. BINDMAN: Thanks. I'll try to be very brief. I think this has been a very useful discussion. I just wanted to make sure, explicitly just to understand, will we have a method to make an accurate estimate of the ongoing marginal costs of sustainability? You made some sort of general statements around it should be sort of less expensive after this large investment.

Will we have a very open and transparent way of communicating that to ensure that the entity going forward -- we have a large public understanding of what those costs are so that it is something we can help to assess the possibility of the public type sponsored research that you are

talking about, and what will be the fundamental basis of being able to do that?

DR. FLEURENCE: The short answer is absolutely yes, we are currently working on cost models as we speak. Part of the challenge is that we have to go back and forth with the individual CRNs to ensure it is an iterative process that works for both the constituent parts as well as the central parts.

We need another couple of months for these to be finalized, and these financial models can absolutely be brought back to the Board and be discussed.

SPEAKER: Common data models and going global, have you all engaged with ICOM, which is a consortium that Michael Ployer and Tom Lee up in Boston are doing to develop international common nomenclature --

DR. SELBY: Bob, we are very involved. PCORI is, on an international standardized set of outcomes.

DR. HERNANDEZ: The answer is yes, just in

terms of other things, Sweden, Singapore, et cetera, we are actually keeping everything very open, and different groups are repurposing.

DR. NORQUIST: All right. Thank you both very much, and we appreciate this, and an ongoing discussion much to be addressed. Thanks.

DR. SELBY: I just wanted to say particular thanks to Alicia who raised the question in the first place and occasioned this presentation on governance. Governance, I think, is something that none of us have thought about enough, very difficult to discuss when we don't know about PCORI's own future.

We told them to sustain themselves with or without us. The scenario is very different with versus without us.

The Council of PCORnet is right now launching over the next six months its own discussion of governance. This couldn't come at a more timely point, and we will look for a venue to have more in-depth conversation.

SPEAKER: I just want to make one final

comment about this, which is two things. One, I think for Adrian and Rachael, the Board is being appropriately engaged now, and we should be, we have to demand accountability.

I've said on the phone to the group and I'll say publicly, we have made an immense investment in the success of this endeavor. It will in a way define us, it is impossible for us to do anything but work as hard as we can to ensure its success.

All of the comments that have been made are extraordinarily good, Alicia, with great respect. You are raising the critical issues. Everyone around the table are, everyone is raising very important issues, and this is a defining moment for the leadership to be able to help PCORnet be successful.

I also want to say I've had the opportunity to see up front and personal the groups working and the staff working and PCORnet and the whole range of individuals, and I just can't tell you how inspiring it is to see people putting in the kind of time and

effort, the talent that has been brought to bear across a broad spectrum of constituencies and stakeholders.

I know the Board knows it, but just to say publicly, it's almost like you're testifying at a Senate committee, you're getting very tough, peppered with a lot of questions, we should be, that's our job, but I just don't want them to leave without a moment of reflection and appreciation because they have so many other things they could be doing on the PCORnet side.

Rachael, bless you, the kind of hours you put in and the dedication. I just want to pause for one second to just reflect on that.

DR. NORQUIST: I think it's like we're the parents, we want our kids to grow up well, so they are going to take a little bit of flack here for a while, but I hope you appreciate that, that is the issue here.

[Applause.]

DR. NORQUIST: We could eliminate the break, but I don't think that is a good idea.

People will start breaking anyway, and then Robin will not have anybody for her presentation. We will take a ten minute break.

[Recess.]

DR. NORQUIST: We're going to get started here. For those of you on the phone, we are starting back. I'm trying to get some other Board members down here. Leah and Freda, you are being called back to the table. Kerry?

Robin, I think the easiest thing to do is to go ahead and start with the presentation. That will calm down some of the conversation.

Robin Newhouse, who is the chair of our Methodology Committee, will now be giving us an update on the Methodology Committee. Do we have other Methodology Committee members here that you want to introduce?

DR. NEWHOUSE: No, not this morning.

DR. NEWHOUSE: Hi, this is Robin Newhouse, and I'm pleased to provide an update of the Methodology Committee's work over the next year, and to update you on the status of the methodology

report revisions.

Over this coming year, there are a number of areas where methodology standards can be helpful to studies that are funded by PCORI. These suggestions have come from the field, input to the Methodology Committee through our public form on the Web, through the work of the staff of PCORI identifying areas where standards would help.

They include a set of four standards. The first one is in meta-analysis. Our intent is to develop new standards for individual participant data and network meta-analysis, and to develop principles for guidance for these kinds of synthesis that ensures a decrease or lack of bias in the conclusions.

The second set of standards will focus on complex interventions. These are standards that have been underway, and we have developed a draft set of standards, and our next step is now to convene a stakeholder group to develop additional methods for guidance over the next two years.

The third set of standards are standards

that we have heard a need for a number of times over the last year, and that includes qualitative methods. PCORI is funding a number of studies that are mixed method studies and the importance of standards for qualitative research is needed.

This is an area where those that are currently on the Methodology Committee don't have as much depth in our expertise, so it's an area where we sought to appoint another advisor to the Methodology Committee that I will tell you about in just a couple of minutes.

The last set of standards will be related to data management, and these were our guidance on standards that will allow reproducible research over the next nine months.

In partnership with other organizations -- actually, we have a meeting tomorrow that we are going to discuss ways that we can reach out to others that are doing some work in this area. The last one being data management.

The four areas of focus for the Methodology Committee are around additional standards for meta-

analysis, individual patient data and network analysis, complex interventions, qualitative methods, and data management.

We sought an advisor for qualitative and mixed methods to help inform our development of the methodology standards, and most recently, we have been very happy to have Susan Zickmund, who is a Professor at the University of Utah, School of Medicine, Department of Internal Medicine, and Division of Epidemiology, join us to help.

She has some deep expertise on data quality and qualitative methods, and will be joining us tomorrow for the discussion about how to move forward with development of the qualitative methodology standards.

The second area that we are interested in seeking some advice is in the area of data quality and large observational dataset management. We need to do a little more work on drilling down exactly the type of expertise we need in terms of advisors for that portfolio.

The methodology report has been revised

based on feedback from public comments. Each section of the methodology report has been reviewed by subgroups and reviewed again by staff and the Methodology Committee work groups.

Right now we are developing a strategy for updating the stories that are included in the methodology report, and we are expecting that we will be recommending a final version for adoption by the Board over the next couple months. The Board then will consider the revised standards and reports for adoption and posting.

You may remember earlier this year we went through a process by which all of our methodology current standards were reviewed. We received public input. We made those revisions. We created a new set of standards for designs with clusters, all of those have now been incorporated into the report, and we are ready to create a final version to bring it back to you.

Let me stop there and ask if there are any questions about our work for the year. Yes, Sharon?

DR. LEVINE: Robin, in meetings, I'm

hearing an increasing call for research that incorporates “real world evidence.” Does that term have any meaning? What does it signify?

DR. NEWHOUSE: I’m not going to give you an academic definition. I’m going to just say what I hear when I hear that. I hear this is the kind of work that PCORI does. The real world evidence is evidence that answers questions that are generated by clinicians and stakeholders and patients, and can be translated very quickly back into the clinical environment. It is evidence that patients need to answer questions that are important to them.

When I hear “real world evidence,” the health systems that I work with are looking for answers to questions they need to answer today for people today, not 5 or 10 years from now, but today, when they are encountering the problems.

DR. LEVINE: It’s not qualitatively different than any category, for example, of the trial methodology, it is not a methodology issue around “real world evidence?”

DR. NEWHOUSE: I would not say there is a

methodology. I would say that we always are favorable to comparable clinical effectiveness study where there are comparators. The qualitative evidence is so important to understand why it works in different settings and situations, how we can best implement it so we can spread the interventions, and make the evidence more available in settings that are not using it today.

DR. NORQUIST: Ellen, go ahead.

DR. SIGAL: Sharon, this is like a hot subject today in research, real world evidence. As opposed to clinical trials that are very pristine, to answer very specific questions, as we know, first of all, few patients, 3 to 5 percent of our patients participate in clinical trials, so that is not real world evidence.

It’s really a much broader cross section of patient populations who really are included, you know, people with diversity, people who are just not part of it, and how you synthesize and get that evidence is another whole issue

There is a methodology to it, but it is

really not relying on clinical trials that are very pristine, to answer very specific questions, that do not include patients with multiple conditions, you know, racially diverse, all these things.

It has become very important, particularly in post-marketing, the FDA uses it a lot for really getting data on what happens to these approved drugs in real world settings.

There is a whole methodology of what it means and how to incorporate it, but it is extremely hot today.

DR. KRUMHOLZ: Real world evidence, to me, is what we have been doing. It's a good package name for it. I have a question for you, which is central to this issue of real world evidence, which is we had a lot of discussion about the ability of observational data to make inferences about causation. We actually sponsored a group to talk about that. The Methodology Committee has spent a lot of time talking about it.

Still a persistent concern that no matter what -- I'm talking almost environmentally, within

our culture and environment, no observational study is going to have the force to be able to change practice.

One of my question is whether or not in this phase of PCORI's evolution we should be focusing -- would it be the sense of the Methodology Committee that if we want to be able to do comparable effectiveness, that we should be focusing more intently on RCTs, rapid RCTs in disparate populations, trying to bring in more diverse groups to participate than we ever have before, and in part, leveraging our relationships that we built over six years in order to do that, but this is what is going to be required if we really want to change practice.

I'm increasingly seeing almost every article published that is observation being forced to include a paragraph that says by the way, this can say nothing about causation, caveat, limitation.

In fact, there is an article in JAMA looking at therapeutic hyperthermia recently, a friend of mine published, nice paper, said this

could be harmful, and the whole conclusion was maybe we should think about an RCT.

We're talking about real world evidence, but we really are at a point where it is just prelude to trying to do something more definitive. I'm really wondering whether or not we should become an RCP machine.

Back to my question to the Methodology Committee, which we depend so importantly on, I think it would be really great to get some of your sense and maybe even more formally their sense on whether this is true.

But for my part, I do not know an observational study in general, short of things like smoking, there have been historically a few instances where it has made a big difference, but in general, if it is something that could be randomized, we should randomize. If it is something that can't be randomized, that's another story, we just have to use the best evidence that's possible. There are many instances like that.

What is your sense in the Methodology

Committee at this point with regard to the use of observational studies where it would be possible to randomize if we had the will?

DR. NEWHOUSE: I can't speak for the committee because there would be great debate about that, I do believe. What I would say is in the health systems and clinical practice, observational data is something that they need to use to direct their decisions every day, when there is no clinical trial to answer the question.

There certainly is a place and a need for both. I think it's a good question to open up to the Methodology Committee, but I think your question is about the mix of the funding portfolio toward clinical trials and observational studies, and what I would say is we certainly could engage in a healthy dialogue, and since the Methodology Committee members are embedded on the committees, it would be a good place to bring that back.

DR. NORQUIST: I think that is actually an important point. One of the things I see a lot, particularly in guidelines development stuff, is

people say well, it's just observation, you know, what's the point. The practitioners are like I can just keep doing what I want to do.

I think at some point somebody needs to defend observational data.

Andy, and then Bob.

DR. BINDMAN: I guess just a little bit more further to this point. I must say that it seems to me one of the most valuable things about observational data is the potential to address external validity versus the randomized trial, which is clearly designed for internal validity.

Yet, I'm a little unclear from the presentation whether the orientation is to try to see if you can have your cake and eat it, too. Are you proposing that observational studies could be refined to the extent that they could become an efficient way to address internal validity?

I think Harlan's point sort of gets that, maybe even with a lot of work it's very hard to kind of pull that off. Is the emphasis or the orientation of the role of the observational studies

mostly to come up with internal validity or to see the degree to which from randomized trials we can in fact see in real world what's going on with regard to effectiveness, sort of the classic distinction that has been made about efficacy in randomized trials versus effectiveness of real world application.

I've not heard an explicit discussion about whether the goal of using the observational data from PCORI is to try to become a low-cost substitute for what you would get potentially compared to randomized trials versus trying to understand effectiveness and how it plays out in the real world setting.

Those are slightly different uses of the observational data.

DR. NEWHOUSE: I would say the role of the Methodology Committee was not to make a recommendation about how PCORI should be funding. That is more the Board's role. Our role was to identify methodology standards that would strengthen the conduct of observational studies.

Many of the standards that were created were to that goal. I'm not sure if that answers your question, and maybe the answer to the question is part of the bigger discussion that we need to have.

DR. NORQUIST: Is it to strengthen the methods for external validity or is it to in fact try to create the capacity to draw inferences about internal validity?

DR. NEWHOUSE: I would say that it moves toward trying to draw inferences for internal validity, while understanding the importance of external validity in observational studies.

DR. NORQUIST: Bob?

SPEAKER: To my maybe naïve mind, randomized trials were the solution for the inability to understand the inherent biases in what we did to certain people was the way we did it. Most of the observational trials were relatively singular experiences.

Today, as we move into the world of big data and we have records on millions of people, a

lot of these experiments have already been done, and just on the sheer numbers, you can make some pretty strong inferences and begin to understand and wash out whatever inherent biases there are, and by the way, there are still huge randomization biases in randomized trials that are not well understood, but when you get bombed with enough of them, you can see them.

I think the ability to begin to really appreciate what we can learn from observational studies. In many ways, if we can provide validation to them, we can begin to influence what happens to people, and we can also really begin to influence how we conduct clinical trials in much more efficient ways by sort of point of care enrollment and conducting trials within this completely external construct of the clinical trial.

We learn by doing, and we learn by understanding the process by which we don't.

DR. NORQUIST: Leah?

MS. HOLE-MARSHALL: Thank you, Robin. Just a couple of comments, especially on the priorities

for fiscal year 2017. I appreciate seeing that individual participant data standard included in the meta-analysis, and I know we are embarked on that now without the standard in place that we are going to do and learn at the same time. That is very helpful, and I appreciate that.

I didn't see anything on NF1 studies. We have funded an NF1 study with a lot of interest or questions about when those are most appropriate and what standards to use if we are going to use NF1 studies.

If it is not in this, is it a subgroup under one of these, or is it something given your other priorities did not make the list?

DR. NEWHOUSE: It didn't make the list at this time, but we have certainly discussed it and are aware of the importance, particularly in the area of rare diseases. Yes, we have discussed it, but just haven't picked it to move forward with it yet.

MS. HOLE-MARSHALL: Would there be something in the interim given being on the

Selection Committee, it is difficult for us when we get requests for funding of this because we have no standards, that we should be looking at using -- perhaps there is something in the interim that we can look to focus on, should we need that. Maybe there are some thoughts around that for us.

My other question, I think, goes along the lines of some of the other Board members, now that we are starting to gather a body of data from the studies that are being published, I'm wondering if the Methodology Committee would consider an evaluation of a select body of evidence that we are producing to help us continue to refine what we ask for in funding announcements.

It may help answer some of the questions around the table, too, of here's what you in fact funded and here are the types of information that could help make informed decisions that are high integrity that we are generating versus information that is either a lot lower in integrity or maybe wasn't as valuable, so we can continue to focus on that.

I know that hasn't been your charge in the past, but I think you are such a valuable group that it would be useful to talk about that.

DR. NEWHOUSE: Just to summarize, I think you are saying we would receive a synthesis of the studies that are funded to make some judgment about where standards could matter or where methods could be improved.

MS. HOLE-MARSHALL: Things for us to focus on, it could impact our funding announcements, for instance, it could impact especially when we do targeted ones of high dollar. If there is specificity that we want to include in the methodology, if we're going to invest $10 million in this study, it better have the following criteria adhered to, to make sure it has the highest chance of being quality work.

DR. NEWHOUSE: We will take that back to the committee. Thanks, Leah.

DR. NORQUIST: Other questions or comments?

[No response.]

DR. NORQUIST: Robin, thank you very much,

and of course, thanks to the committee for all the hard work I know all of you are doing. Thank you.

Our next session is a special kind of anniversary panel. Joe has organized this and is going to lead it. I don't know where our distinguished guests are. I saw them earlier. Steve Lipstein and Gene Washington.

Gene, we were joking. We thought you were going to come in in costume for Halloween.

DR. SELBY: Good morning, everyone. Welcome to the last town hall meeting of this campaign season.

[Laughter.]

DR. SELBY: I don't know whether I should refer to these guys as the candidates or the defendants, but here they are. They're indulging me actually with a set of questions that I contributed to as well as others. We are at six years. These two gentlemen had the leadership role with the Board of Governors in September of 2010, and had to figure out a lot of things from scratch, had to make an organization out of whole cloth.

It's a particular treat and an honor to have them both come back, and I want to thank you, and I think it must say something about how much they still care about PCORI, that they are here with us today.

The fact checkers are on line, I believe. Is that right? My COO, Regina? You can watch on the screens at home if there is a deviation from the truth. I don't expect it. We don't encourage it.

Opening remarks. Would either of you like to make a little opening comment? Then we are going to turn it over to the audience, so probably people from all over the country will be asking questions today.

DR. WASHINGTON: First, I am Gene Washington. I served as the first chair of the Board of Governors for PCORI. I am currently at Duke University.

MR. LIPSTEIN: My name is Steve Lipstein. I was Gene's sidekick as the first vice chair on the PCORI Board. I am currently -- still the President of BJC HealthCare in St. Louis.

DR. SELBY: Great. We will go straight to the audience. I have Ms. Nick Wilson.

MS. WILSON: Hi. I'm Nick Wilson. I am from Sonoma County, California. my question is what did you as the Board make of the name PCORI was given? It's notable that the name PCORI doesn't reference the clear mandate of comparative clinical effectiveness research, and the legislation provides almost no instructions for conducting patient-centered outcomes research.

DR. WASHNGTON: First of all, I didn't realize I had skipped the introductory comments, but I'll just say I'm delighted to be back. I have truly missed this group and the collaborative spirit that always embodied our gatherings. Good to see all of you again.

For me, even though you are directing this to me and Steve, this to everybody in the room because you were all there, but to me, I thought it was an inspired choice of names. The reason why was because it in a very succinct way provided us with multiple different anchors.

It provided us with the anchor of patient-centered, and if we had just been talking about comparative or clinical comparative effectiveness research, it would have been a little bit more difficult for us to stay as closely linked as I think PCORI has successfully done over the past six years.

It also put the emphasis on research, in terms of the aura, and then third, importantly, it put emphasis on outcomes, and that we were conducting research, not for the sake of research, but really for outcomes that mattered most to patients.

I don't think that is captured by the phrase "comparative effectiveness research," and it was for PCORI to link comparative effectiveness research to PCORI rather than vice versa. I happen to believe the organization has done that exceedingly well.

MR. LIPSTEIN: I would add, first of all, Russell, you are my replacement, right? There is somebody else who is new, too. The two of you

should just know that you have joined an extraordinary group of people that Gene and I came to not only think of as fellow Board members, but really colleagues and close associates, and we got to know each other in the formative stages of PCORI, and our personal relationships are probably equally as strong now as our professional relationships.

By way of introduction, I would add that when PCORI was formed, Gene and I didn't know each other. We had never met any member of the Board. One of the first things I did, and I will leave this as a present behind because I brought all my remaining hard copies of the PCORI statute, and the Sharpies, where we actually went through the statute, I brought you a spiral bound copy of the statute.

We had to go through it, and to say there are some inconsistencies in the statute would be as Sharon just said, an understatement.

For example, PCORI was supposed to be established as neither an agency or an organization of the Federal Government, and yet, the first two

Board members that were named to be on this Board were the Director of the NIH and the Director of AHRQ, and okay, we are supposed to be independent of government, but our first two Board members lead two of the leading health care agencies in the government.

The second thing it said was we had to be a not for profit corporation incorporated in the District of Columbia, but Gene was living in Los Angeles and I was living in St. Louis.

Literally, the only thing that we really felt like we had to go by in the initial days was the statute on how to get started, and how to look at both what was in the name, as your question implies, but also how we were supposed to go about organizing and establishing this Board.

Some of you will remember the very first meeting in Los Angeles was paid for by BJC HealthCare because we didn't have any money in the bank at that time.

We formed ourselves very quickly. We were appointed the end of September/early October. We

convened in November. By January, we were working on the first two key provisions of the statute. One was to establish national research priorities, and one was to establish a research agenda.

While we were doing that, we recognized that we probably would benefit from having some staff. We literally launched our search committee in January of 2011 that brought Joe into PCORI in July of 2011.

All that is by way of just some background to say that we were actually working very hard and making a lot of decisions as quickly as we could be using this not clear statute as our star, which is why we went through and highlighted it very, very extensively at one of our early meetings.

What I remember came out of that early meeting was the high ground among all of us was the word “patient,” whether we were surgeons, cardiologists, health services researchers, whether we had been in medical school or not. We had and still have psychiatrists on the Board, which is really important. We had a couple of lawyers who

were actually functioning as our general counsel because we hadn't retained legal staff yet.

Whatever we did, when we went through the statute, we all could come back to the patient as a moral compass and a high ground around which we could build our national priorities and our research agenda.

DR. SELBY: I failed to say a couple of things. One is one purpose of this is to remind all of us, and particularly our two new members, of that early history and how we got to be the way we were.

And second, really would like to invite other Board members, as we go from question to question, if you have something to add on this question about how did the name that we were given affect us, or what did you make of it when you first saw it, feel free to chime in before we go to the next question.

Sharon?

DR. LEVINE: Sharon Levine, Board member. I think one of the things I think has stuck with me, we had a very, I would say, intense discussion about

patient versus person, and whether in fact by what the statute said we ought to be thinking about people in the broader sense of the word and not just those who are “patients,” which really is defined by an encounter with the health care system, and if in fact, the country and taxpayers and payers who are funding this institute were to get the best return on the investment of those dollars, we would be looking beyond illness and health condition, and looking at interventions and approaches that improved health in the broadest sense.

Speaking of the statute, I think what we could do is somewhat constrained by the fact that we had six years to show something -- I’m sorry, nine years, to show something for our efforts.

I think below the surface is should we get reauthorized and should the world turn in our favor, it would be lovely to begin to think about a broader application of comparative effectiveness research in its broadest application.

DR. SELBY: I would say, Sharon, most of you will remember we had lengthy discussions about

that, and it was reflected in the mission statement, where we say PCORI helps people. That word was underscored early in the statement as the broader context that you are describing now.

Harlan?

DR. KRUMHOLZ: Harlan Krumholz. It's good to see you guys, and we are sorry you left the Board.

I just want to say one thing, and I'm curious about your reaction to this. I thought one of our major accomplishments in the beginning was to say we want to be distinguished by doing research differently, and we wanted this perspective to be integrated into everything we did, not to be an extra, not to be extracurricular, but for the work we did.

As I reflect on it now at this stage, because I think we are at an important juncture with those nine years that are coming up soon, we may not have spent as much time on the comparative effectiveness side.

Like I said, I'm really proud of the piece

that we did about the patient part, but maybe the name also put us in a position where we didn't think as intently about the comparative effectiveness side and what the body of work would look like.

I say that now because you can hear from my prior comments where I'm wondering whether the Board should now -- phase one was really making sure we went to the community, making the strong relationships, integrating the processes into everything that we did, making sure people were in the study section, making sure we were listening to priorities, really establishing that as a baseline, influencing the country.

I would say we have changed the conversation about research, even as you look to what Francis has done with PMI, that is very much a reflection, I believe, of what was begun here with regard to how people could play a central role with the center of research.

I see it everywhere. I even believe the real world evidence is in part a reflection on talking about real people in everyday life.

I'm thinking about the need for us to pivot, make sure we pay enough attention to creating that body of work of the A/B comparison, the A/B/C comparisons. No one is going to say you're just like everyone else with the way we do it, but that we need to do that.

I think the name -- if I think back to that time, I just wish in a way I had thought more about let's do it together, and we have a big body of work that we funded, not to mention that, but wondering whether or not we should pivot.

I wondered what your reaction is in thinking about that.

DR. WASHINGTON: First, I want to remind you, Harlan, you took a pretty strong position back then, too, making the same point that you're making today. Others will no doubt recall that. It was appropriate.

I haven't followed as closely as obviously members on the Board, but I think after six years, it is probably the time to reflect on the balance, and what the allocation of resources should be going

forward, that builds optimally on what has already been established.

DR. KRUMHOLZ: I do take full responsibility. That's why I said as I reflect on myself, this is a great Board, the staff is doing a great job. I'm just saying where we are now, I just want to make that clear.

I was 1,000 percent and I'm still 1,000 percent in on the idea of people being at the center, no question, I'm not wavering one bit.

MR. LIPSTEIN: What I would add is when we came together, not only did we have to set up all the infrastructure around PCORI, but we had no what you would traditionally think of as Board by-laws or committee structure.

After our first two meetings, when we listened to all the input from 21 unique voices on our Board, we came up with two committees. One was the program committee or the program development committee, which is really going to focus on the research agenda and the research priorities. Rick, I think you chaired that committee in the beginning.

You were a lot younger back then. Sharon, I believe you chaired the first version of the engagement committee.

Those were the two things that came out. We wanted to do research but, Harlan, when we talked about doing research differently, it was always about engaging patients, and not only in developing the research questions but getting them to be more engaged in the study methodology, and importantly, being a part of understanding the results and disseminating the findings.

We set up those two committees, and then we had a third committee, which was finance and administration, because we still didn't have a payroll, budget, lawyer, or anything like that.

That was the evolution for about the first two years of our committees. Then you may remember we added a committee after two years called the research transformation committee. I think Freda, you chaired that, or you used to -- still do.

That was part of that, we were pivoting at that time a little bit, Harlan. Now that we have

our priorities and our agenda, and we have focused on engagement, how do we really do research differently?

Out of that research transformation discussion came PCORnet, which was a big topic of discussion, Gene, this morning. Then as part of that transformation journey, the Board had gotten more and more comfortable with doing what they called “large pragmatic studies.” I always thought everything we were doing was pragmatic, but I was a non-scientist at the time.

One of the real things that helped me grow on this Board, by the way, was after I stepped out of my role as vice chair, I convinced Kerry and Gray to appoint me to the science oversight committee. That was very educational for me, because I had never been -- a non-physician, non-scientist to be put on the science oversight committee, just to hear the dialogue and to understand the issues was really, really helpful for me.

It also reflected that continuing journey to where Harlan is making his point, which is we

have to get more comfortable now with targeted studies that answer specific questions, is this better for me or is that better for me.

DR. SELBY: We have a lot more questions from the audience. Ellen?

DR. SIGAL: I'm going to be brief, but I just want to take my brief time to thank both of you, because the extraordinary work that came on us was just incomprehensible. I don't think anybody knows what it was like in those early days, no bank accounts. There are funny stories about even how we could get a bank account.

It was a full-time job. It was consuming. Great thanks to both of you for doing what you did to set us up and work 24/7. You should be very proud. We have come a long way, and we could not have done it without your leadership, time, and commitment. So, great thanks.

[Applause.]

DR. SELBY: We have Ms. Sue Sheridan in the audience with a question.

MS. SHERIDAN: I want to share that for the

past almost five years I have been very proud to share the PCORI mission with probably hundreds of audiences. I'd like to say the mandate didn't require that patients and caregivers and other stakeholders are engaged in our research, but this Board took PCORI to the next level, and I think actually ended up with a very courageous mission.

I want to invite you to share with us how did the Board actually come up with that mission?

DR. WASHINGTON: Who was on board for the mission statement? I saw Harlan Weisman here earlier.

SPEAKER: He's right next to you.

[Laughter.]

DR. WASHINGTON: Now you can see why we called it the old timers session. Harlan was very involved. We set up a task force, a team, to actually write the mission statement. You will recall this. Harlan will remember that every word was selected very, very carefully.

We had a group of people on the Board who really felt until we could articulate our mission

and write it down and get everybody to say this is what we are about, that it would be hard for 21 unique people -- sometimes they refer to this Board as a stakeholder board, but that is not really -- there is no recognition of the term “stakeholder” in the statute.

What really you had was 21 very, very smart, caring, intelligent people who all think about what PCORI could do and how much benefit it could provide a little bit differently, which is why there are 21 voices, and getting them altogether on the same page, Sue, was really important.

Harlan and I spent time on the phone together taking out this word and recommending that we add another word, all trying to get 21 people to say okay to this.

MR. LIPSTEIN: I certainly remember that. We did two things. One was the mission, who are we. The other thing was the vision, where are we going. What is that destination. I thought both of those were really important.

The other thing I would say, you have

brought it up a couple of times, we were 21 very different individuals, unique individuals, but we represented multiple stakeholders. I remember in the early meetings, Freda, Rick, and I decided as the industry people, we better lay low, and I think Ellen reinforced that, keep it down.

[Laughter.]

MR. LIPSTEIN: One of the problems with health care in the United States, certainly even more so back then was the fragmentation. You have all the multiple stakeholders in the room, and there was a lot of finger pointing, not on the Board, but among various stakeholders.

I think what really happened is this Board gelled. We found out that despite our various perspectives and maybe viewpoints about what needed to be done, we shared in common the idea that one, patients were at the center, and that we wanted to have an important role in improving the health of Americans, and helping them make their decisions. That really unified us.

That debate around mission vision, which

seemed to go on endlessly, and wordsmithing, I think was one of the fulcrums of helping us unify together and really serve as a model for the nation and the idea that you could take all the various stakeholders involved in health care, put them together, and put them around a common goal to come up with really important solutions.

DR. SELBY: There is a question from Lori Frank, which is similar to what Steve just addressed. Ms. Frank?

DR. FRANK: Hi, Lori Frank from Kensington, Maryland, and I am here today as Dr. Frank Enstein. I would like to thank you for your service to PCORI, and I do want to follow up on the multiple stakeholders on the Board.

What was your view of the legislative intent there, and do you think that intent has been realized?

DR. WASHINGTON: I would comment first on that and say yes, I think it has been realized. I interpret it as ensuring that in fact it truly was a multidisciplinary group of stakeholders from diverse

backgrounds and diverse perspectives, and range of experiences being brought to bear on the questions at hand, which were about how do we produce information that is useful for patients.

I think the PCORI Board as a group serves as an exemplar, that it really can be done, and it can be done at a national level. To the person, and Harlan just touched upon it, I felt that each individual stayed focused on the higher aim of PCORI, which was to use these resources as effectively as possible in order to improve health care delivery and improve health outcomes.

As a Texan, we use the expression “Check your guns at the door.” I always worked with the assumption that each member in fact did that, when they came to the table, they came to the table as a Board of Governors of PCORI. Yes, perspective was there, but there was not one single member that I recall on any occasion dug in deeply over representation of some constituency or some stakeholder, and I’ve seen that continued the last six years.

I think intent was right on target, and I certainly think the Board of Governors have lived up to the promise of bringing this kind of diverse group together.

MR. LIPSTEIN: I just looked at that language because it is always helpful for me to remember. It says I was appointed to the Board as a representative of a hospital. I certainly never came to Board meetings feeling like I represented all 5,000 hospitals, big and small, teaching and non-teaching, urban or rural, pediatric or adult, in every state of the Union any more than Kerry, you felt like you represented every single insurance plan in America.

What I think we tried to do was use our different lens to say okay, what are the issues that are most important to patients or to beneficiaries or to patients in our particular disciplines, what would be most important to those patients.

I think as some of you know, my office back at BJC is in the same building with the resident clinics. I wanted to be there because it gave me a

chance to actually see and engage with patients every day in a way that non-clinicians get to do, which is usually providing directions or giving assistance at the elevator, but these are also the patients who are the most vulnerable in our community because many of them don't have insurance and many of them don't really easily know how to navigate the health care system.

One of the lens I tried to bring to my service on the Board was not just any typical patient, but patients who really were living in poverty and under difficult life circumstances. Some people brought to the Board the lens of patients who were suffering from cancer, or cardiovascular disease, or mental illness.

Realizing that there is a huge diversity of patients and patient issues, patient questions, patient problems, I reviewed the stakeholder nature of the Board to try to be inclusive of all those different patient perspectives.

DR. SELBY: Does anyone else on the Board want to comment on this question? Dr. Zwolak?

DR. ZWOLAK: Thank you. I'd just like to follow up on what Steve mentioned and ask a question. In the early days, we met in Los Angeles, we met in St. Louis, we saw all sorts of people, patients, patient groups in St. Louis. We went to New Orleans and went to indigent clinics and heard some incredible stories about the care provided in New Orleans. We went to Jacksonville, I think, and stayed at the worse hotel there ever was.

[Laughter.]

DR. ZWOLAK: We heard important stories. We really engaged people. We engaged all sorts of people, all the ranges. Now we have become sort of very bureaucratic. We sit here, we meet in Washington. We rarely get a public comment. We have gone quite to the other extreme.

Is that just a process of our evolution, was one right and the other wrong, or is this just how things should flow? From the perspective of someone who has watched us, both of you, from legislation to today, were we right then and strayed too far away now, or are we doing things right?

MR. LIPSTEIN: I'll start and then let Gene go. I think what we were doing back then, we were trying new things. We were trying to figure out, okay, we gave staff the opportunity to help us figure out ways to engage people differently. We were just finding our way at that point.

As you know, we were in different cities around the country, and we wanted to just invite various patient populations or various patient advocacy groups to share with us their lens on what were the most important issues affecting patients.

I used to share with Gene on our daily phone conversations that one of my big concerns was that I viewed patient advocacy differently than patient engagement. When we would have normal meetings like this, the people that would come to the microphone were coming with prepared statements, written by either the disease association that had sent them, and the example, you may remember I gave you was -- Rick Kronick shared this -- we both were supporters of the National MS Society, which is a patient advocacy group. Both of our wives had MS.

We know patient engagement and patient advocacy are two different things.

What we were trying to figure out is how do we get past the advocacy groups who were lining the walls of our early Board meetings to touch real patients with real medical conditions and problems.

That's what we tried to do, and that is what I think Sue Sheridan's world has -- I can't see her now, she is behind the camera -- I think that is what your world has become all about.

It turns out there are probably more sophisticated and efficient ways to reach real patients than what we were trying to do back then, but it's no less important.

DR. WASHINGTON: Bob, I think at the time, we were weighing a couple of tradeoffs. One tradeoff was the desire to have that submergence experience up close, personal, and the cost, the cost in terms of resources, but also time. Having said that, I share the bias that there is no substitute for that on occasion.

If you're telling me you meet in

Washington, which is the case all the time, I would say I would as a Board of Governors would be pushing you to get out every now and then, whether it's once a year or once every two years, whether it's an annual meeting at some site that gets you away from Washington. I would be encouraging that.

DR. SELBY: Sharon Levine.

DR. LEVINE: Just to give a broader perspective on this, we recently had a face to face meeting, all day meeting with the engagement dissemination -- I forget the rest -- implementation committee, EDIC, and heard a phenomenal presentation over a period of six hours of the degree to which PCORI was touching the lives of real people in real communities.

The staff has done an extraordinary job of extending our reach into the community. I think in the beginning all we had was us. That was our only mechanism of engaging with people and trying to get, as Steve said, beyond advocacy to engagement.

I came away from this last meeting really totally wowed by the degree to which the staff, Jean

and her team, have just touched the lives of hundreds and hundreds of real people, real patients, and real communities, by taking PCORI to where these folks are.

I think we said at the end of the day it would be lovely for the Board to hear actually what we heard because I think it was a marvelous story and very affirming that we have in fact on this dimension of our mission and our charter really lived up to what we could do.

MR. LIPSTEIN: First, I'd say those early trips were other places, too, like New York and Seattle, and were some of the most meaningful -- I had some of the most meaningful conversations and participated in some of the most meaningful discussions with the multiple stakeholders, and really got a glimpse of what health care is really like.

I learned that I live a very insular life, and through the various things I've done in my life, I've always had instruments, because I'm a physician, I know how to pick good physicians.

Really hearing from people -- you know, we used the term “real world” earlier. Seeing real world in the United States really shattered a lot of things that I thought were true that are not true, and it was very important.

I think what you just said about the fact that we have people who do that now. It is part of the evolution. When we started, we were the organization. That’s all there was. Now we have a real institute and real professional people who go out and engage all the time.

My answer to Bob is I think it was part of the natural progression and evolution, but I do agree with Gene. It is very healthy to get out there and see what is really going on.

DR. SELBY: Andrew Bindman?

DR. BINDMAN: Hi. This is great for me because I wasn’t here in the beginning. I came after the original seven days of creation.

[Laughter.]

SPEAKER: It took longer.

DR. BINDMAN: Okay. Steve, I was struck by

some of your opening comments about we are supposed to be separate from government, but then the first two Board members are from government, so I'm one of those representatives now.

Has that reflected some ongoing ambivalence, you think, that there is about PCORI and its relationship? I guess I'm particularly interested in any of the discussions you all had in the beginning about how PCORI should engage with government partners.

There is, as you know, in the legislation some comments about thinking about relationship roles with NIH and AHRQ. I wonder if you could enlighten me a little bit about some of the discussions that were had about how to use that relationship and any reflections you would have about how that relationship has evolved vis-à-vis execution of the work, staffing, and things like that.

MR. LIPSTEIN: It's a great question, Andy. One of Gene's early suggestions for how to help us understand that was for us to go visit with the

people who wrote the legislation, and then what we found out is there were more people who wrote the legislation that was actually humanly possible. We visited with both House and Senate leadership on both the Democratic side and Republican side.

What I think we walked away with was realizing that the legislation, if it was confusing or conflicting about the relationship between PCORI and government, it was because there wasn't agreement inside the government at the time the legislation was actually written.

There were some people who thought $3 billion over 10 years should reside within AHRQ. There were others who thought it should reside within NIH. There were others that thought independent from government meant not independent from the Senate but independent from the House.

I walked out of there -- I remember, I said to Gene and other members, is this how government really works. He looked at me and he just kind of smiled, you know, that wise smile he has, and we realized -- at the time, Caroline Clancy was filling

the Board seat you are in, Francis was still in his seat.

We just forged that working relationship the way it felt comfortable with the Board and comfortable with them, knowing that in this town, biomedical research, health services research, exists within a sociopolitical economic construct, and navigating that construct is not always easy. It is very complicated.

We have had both Francis' wisdom and now your wisdom, and Bob Jesse along the way representing the VA, that really helped us to navigate those relationships. I think we ended up in a good place.

We clearly didn't get clear direction from either the statute or from the people we visited on the Hill.

DR. WASHINGTON: I remember one Board meeting where Christine had written public funding announcements for the pilot projects. We had no way on earth that we actually were going to be able to go through those and be able to figure out which

ones we should grant, we should fund.

Francis Collins said, and I remember these words, “I’ll be the plumber.” That is one of the first relationships we built.

DR. SELBY: Bob Jesse.

DR. JESSE: Bob Jesse, Board. I wanted to reflect on what Harlan and Steve had said about our early visits in the communities. The thing that struck me most about that was irrespective of the disease people had or their station in life, the one common thing everybody wanted from the health system was respect.

I think our presence with them showed that we as a new organization actually respected them. We had a couple of social faux pas in there, I think. We learned a lot. We all learned a lot. I think that lesson really is foundational to everything that has happened in PCORI since.

Whoever’s brilliant idea it was back in those days to have those meetings, I think it was a very positive investment but one whose value is not easily understood by those who weren’t there.

DR. SELBY: We will move on to the next question. Mr. Andrew Hoo.

MR. HOO: Before I jump to my question, I just wanted to apologize on behalf of those of the folks who wrote the authorizing statute for all the confusion and all the errors in the language.

My question is more about some of the key pressures you guys faced at the outset, from the various stakeholders and from Congress. I'm sure some of those were conflicting in more of the decisions and choices you guys made to address those.

DR. WASHINGTON: Where do we start? There were pressures all around. This sounds like boring stuff because it is, but I want to give it some context.

At the time when we were trying to launch PCORI, we already heard it was whole cloth, no clear roadmap, somewhat not confusing but not very clear in terms of direction from the legislation. Widespread opposition to the actual passing of the legislation. Major budget crises in Congress, and

an attempt very early on, deliberate, to derail all the efforts to launch PCORI.

Some of you remember at our early meetings, we had guards at the door. When I would get up to go to the restroom, the guard would go with me. He had been cued by the security company that people were not to get to me. It paints a very different picture from the setting we are in now, but that is how the moment was, I mean more broadly.

Our first success was just to avoid lift off failure, because so many forces were aligned to really achieve that particular objective. Fortunately, there were the forces aligned to help us with that lift off. That certainly included the Board to begin with.

Ellen, the same way you recognized me and Steve, I really want to recognize each one of the Board members who were involved in those early days because each Board member worked as hard as Steve and I, you know, relatively speaking, and given that they weren't in a leadership position, and we always knew we could call on them seven days a week, and we

did often call on them seven days a week, and there was always a response.

As Steve said, there was no staff. The Board was the staff for literally the first year. They would joke saying, you know, when I got that call, they didn't tell me that I was going to be in this deep and this busy, committing this number of hours, but no one complained and everyone delivered.

That was the tension just to get it off the ground. From the beginning, people wanted victories. On one hand, they wanted to thwart any effort to launch it, and at the same time wanted victories within the first two or three months. When we would go, as Steve said, to Congress or we would go to different constituencies, they wanted to know when is the first recommendation going to come out. Others wanted data. Others wanted funding even before we had mechanisms.

There was real pressure early on to have some victory. Talk about pressure and tension, early on, there was pressure around whether or not we would include costs. I suspect some of that

still is. There was a large kind of cross section of individuals and groups that felt PCORI couldn't be successful, despite the mandate we had being relatively clear unless we took on costs in some meaningful kind of way.

Attempting to respond to those concerns and the criticism while were also moving forward to focus on patients and on the research and outcomes created its own kind of pressure and tension.

Andy, back to your question. I wouldn't call it a tension, but we had open discussions about the role of AHRQ and NIH and PCORI relative to PCORI's independence. As Steve said, we would hear very clearly don't waste any dollars, we want you to also demonstrate that you are just not another AHRQ or another NIH. That was pressure for us to create the right balance.

I would concur with Steve, and the same way Francis stepped up, Caroline stepped up, Gene worked with Caroline in those days, and I felt like the evolution was timely and was effective.

There was that tension there and pressure.

I felt like we got that right as well. There has always been not the pressure but the tension that Harlan alluded to about how much emphasis we put on research versus how much we put on patient engagement, which will always be there.

There has always been that tension about how much research we do related to more of the observational end versus experimental. Those pressures were there then and those pressures continue to be there today.

Finally, just related to the research, there was pressure to make the big bet versus being more incremental. Many of you will remember those discussions. What was the term we used to use?

SPEAKER: Big rocks.

DR. WASINGTON: That's right. Move the big rocks. Did that come from you, Harlan? I thought it did. We were going to move the big rocks. In some regards, PCORnet certainly represents a big bet from my vantage point that is paying off with real potential for even more significant contributions.

Those are just some of the tensions that

were bubbling beneath as well as above the surface.

MR. LIPSTEIN: In the first nine months, there were two big tensions that Gene just characterized. I'll summarize kind of what he said and replay the pressure. Christine Goertz will remember the words "get the money out the door." It was because we were deep in recession, there were people around this Board table that wanted us to get the money out the door.

There was another really important group in the PCORI mix that didn't get on board until March of 2011, which was the Methodology Committee. They will remember they met in the living room of my home in St. Louis. That's when we learned Steve Goldman could sing, by the way.

Until we had the scientific vigor and the methodological standards, there were other Board members who just didn't feel comfortable pushing all that money out the door.

The second thing where we clearly felt pressure on was to get a staff. When Joe almost withdrew from the candidate pool, I was calling Gene

crying and saying Gene, you have to get him back in the pool because he's everybody's first choice, and we have to get him back in the pool. That is when the famous call came. Joe, our country needs you.

DR. SELBY: I'd add a third, and that was a Supreme Court case.

MR. LIPSTEIN: That wasn't until 2012, and what happened in 2012, you will remember, we were worried that we wouldn't be able to get out money out of the United States Treasury into the PCORI Trust Fund, and we had already hired staff at that point. Yes, we did make a decision to make an early withdrawal from the Treasury into the Trust Fund.

When the law turned out to be constitutional, we tried to put the money back into the Treasury, and that was not as easy to do as the other way around.

DR. SELBY: Alicia Fernandez.

DR. FERNANDEZ: Thank you. I have a question for Gene. I only came onto the Board after Gene left, but I know Gene because when I was an intern early on in my life, I think Gene was one of

the foremost faculty at UCSF, and among his many talents was he was extremely committed to disparities research and to equity.

My question centers on that. PCORI has done a lot in terms of addressing the disparities portfolio and has an active portfolio of research. Nonetheless, many of the big issues that trouble the health of vulnerable people in the United States need to be addressed with research, but always fall into a comparative effectiveness model of comparing therapeutic A versus therapeutic B.

I guess as you stepped away from PCORI and had a chance to reflect over the last few years, what have you thought looking back in terms of PCORI's contribution around equity and health, and more importantly, any thoughts you might have around going forward in how PCORI can contribute even more in that area?

DR. SELBY: Gene, before you answer, let me just say that we have just about run out of time. I think this will be the last comment from you and from Steve. Let me invite you as you answer

Alicia's question to also just any closing thoughts you want to leave with the Board for prosperity.

DR. WASHINGTON: Alicia, I reflect on those visits we made, and particularly in New Orleans. Some of you remember, we went into the heart of New Orleans. We felt like we had kind of touched to some degree the soul of the problem, at least I did. I still remember those days.

What I learned from that and how to respond to your question, to the degree that we really -- I believe we are changing the conversation, we are cracking the code around research being more from the patient perspective, then I think we are helping to address some of the disparities.

The individuals who have the most difficult time in the health care system are the vulnerable population. Those are the ones who don't understand the material. Those are the ones where the families are not included or don't feel like the decisions that are being made necessarily reflect their values.

To the degree we are getting the research

more from that perspective, I think we are contributing to improving that problem. I think we should continue to do that. Again, whether it is in the realm of more observational studies or whether it is in the realm of experiments.

What I would leave in closing as I thought about where PCORI is now, and that is even before I heard the discussion this morning about balance between RCTs and observational studies, I heard a little bit about PCORI in the update this morning, and I think PCORI is very similar to what I was saying with so many other big projects around the country that is amassing just mounds and mounds of data, and what I don't see right now is big, big projects really analyzing it in a way that is being used to really change care, and eventually improve health.

I see that the next big push, and PCORI can play a role in that, is ensuring whatever kind of analytical studies or evaluations, there is better use of all the data that is being created, not just for research but actually for improving care and

improving health.

MR. LIPSTEIN: My two parting thoughts. One would be, you know, I have spent a fair amount of time the last year back home in St. Louis trying to think about how we improve the odds for segments of the people who live in our community, a lot of which has come about as a result of what you all read in the newspaper related to Ferguson.

In my PCORI experience, I think that the purpose of this institute is really to improve the odds that people in our country will get to a better health outcome. Some of that does involve equity. Some of it does involve head to head comparative analysis of two different therapeutic options.

Just keeping in mind how do you improve the odds of improving patient outcomes, and not everybody has equal odds at the get-go. That is kind of take home message number one.

Take home message number two, I spent the last year of my PCORI service on Dr. Zwolak's work group called Application Enhancement Work Group. One of the mysteries for me as a member of this

Board was always why the questions we were asking, that we thought were the most important questions in America, weren't coming across in response to our broad application solicitations.

Harlan and I used to tease each other back and forth on Tamiflu. I always wondered why were we getting five research grant requests to study Tamiflu. We were sitting in our Board meeting. Bob and I went through this, and I think, Vic, you were on that work group, too, we went through this process and staff really helped us, and I kept thinking why aren't we getting the kinds of applications we want.

We kept thinking what are we doing wrong. Then I wondered, maybe there isn't as much demand for answering the questions that we are asking as we thought there was. I think that is something the Board needs to take on as it looks to the future, which is there is a disconnect between the top research questions that we think need to be asked and answered, and what will come from the research community in response to our RFPs.

Good luck.

DR. SELBY: Well, I want to thank both of our candidates --

MR. LIPSTEIN: Joe, can I have the last word?

DR. SELBY: You certainly may.

MR. LIPSTEIN: Everyone involved in PCORI, Board of Governors, the staff, the Methodology Committee, should be proud.

DR. SELBY: Thank you both.

[Applause.]

[Whereupon, at 12:37 p.m. a luncheon recess was taken.]

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

[1:01 p.m.]

DR. NORQUIST: We're going to get started. For those of you on the phone, we are back now. Larry Becker will introduce our next session.

MR. BECKER: Thank you very much. Ted, are you on the phone?

MR. CHEATHAM: I am here.

MR. BECKER: All right. Thank you very much. We have three individuals who are experts in their field. Thank you for coming today and spending the time. I know you flew in from New Hampshire to be with us at the last minute, so thank you for doing that. Ted is in West Virginia. James, thank you very much for being here.

Let me just give you some brief comments about each of the individuals. Ted is from the West Virginia Public Employees Insurance Agency. He's launched HMOs in Los Angeles and Mississippi. He's been involved with acquisitions and mergers in West Virginia. He's a former CEO of several commercial health plans. That is his background.

Kathryn is with the American Benefits Council. She is a senior counsel there. It represents Fortune 500 companies and 100 million Americans. She is involved with assisting members like Xerox Corporation with health policy, health care reform, regulations affecting plan sponsors.

James Gelfand is with ERISA Industry Committee, Senior Vice President there. He has done a lot throughout his career prior to coming there in April. He worked at the U.S. Chamber for a time where I met James. He was also counsel to Tom Coburn and Olympia Snowe before that.

I think we will get started. Jim, do you want to kick it off?

MR. GELFAND: Members of PCORI Board of Governors, thank you for this opportunity to present on behalf of the ERISA Industry Committee, or ERIC, for short. ERIC is a non-profit organization representing the nation's largest employers that maintain health care, retirement, and other employee benefit plans covered by the Employee Retirement Income Security Act of 1974, ERISA.

ERIC is the only national association that advocates exclusively for large employers on health, retirement, and compensation public policies at the Federal, state, and local level. ERIC enhances the ability of its member companies to provide high quality health care benefits to millions of active and retired employees as well as their families.

These benefits help ERIC members to attract and retain talent and maintain a healthy and productive workforce. Each ERIC member must have at least 10,000 employees. Many have 100,000 or even a million. Plus, the number of covered lives under each of their benefit plans is usually much, much higher, as you take their families into account.

ERIC's members, which sponsors the absolute largest private group health plans in the country, are committed to and known for providing high quality, affordable health care. Our members expend considerable resources to maintain insurance plans that cover many disparate populations.

These plans provide health care to millions of workers, retirees, and their families with the

highest standards of quality, cost containment, and effectiveness.

As you can imagine, ERIC's member companies have long been on the cutting edge of innovation in the health care space. It was large employers who first took a chance investing in care coordination creating incentive programs for employees to get and stay healthy, and steering plan beneficiaries to centers of excellence, where they would receive the best, most efficient, and most effective care.

ERIC's members voluntarily made investments in health information technology long before the Federal Government was involved. Even now, ERIC members are constructing accountable care organizations that are more advanced than those envisioned for the Medicare population in the Affordable Care Act.

We could discuss this until I'm blue in the face, but the point I'm trying to make is that ERIC's member companies have taken an extremely proactive approach to managing and improving the health of tens of millions of people for whom we

provide health insurance.

There is a myriad of reasons for our interest in the health and well-being of our employees, from simply caring about the people who we work with, to encouraging better productivity and discouraging absenteeism, to giving workers the peace of mind they need to focus and maintain a positive outlook.

Employers have a stake in employee health, but that is not all. ERIC's member companies are all self-insured. That is to say when an employee goes to an emergency room, it's not the insurance company that pays the employee's bill.

Sure, we have an insurance company that acts as a third party administrator. They set up provider networks. They do the paperwork. They negotiate rates. Ultimately, it's the employer that pays the bills.

Employee health for ERIC members is more than simply a matter of goodwill and productivity. It is a bottom line imperative. This is a good lead up to comparative effectiveness research. ERIC,

along with many of our most active and vocal member companies, as well as our friends and colleagues in the employer trade association community, have a long history of supporting comparative effectiveness research, besides the general transparency and health care position, we also have a more immediate need.

You see, large employers are increasingly offering consumer driven health plans in which employees bear a greater responsibility for choosing providers, care regimen, medications, and other health services. Employees need access to robust data in order to make informed decisions.

Comparative effectiveness data is high on our ranking of what's needed to meaningfully differentiate between care options.

When the Affordable Care Act was being negotiated, employers had a great interest in the creation of a body to conduct comparative effectiveness research, by requiring all payers to contribute, we could eliminate the free rider problem and build a centralized clearinghouse to

serve this critical need.

However, since the ACA's passage, a number of new questions have been raised about what our investment has yielded thus far, and that will be my focus in these remarks.

First, on PCORI's work. Major employers had one chief goal in funding comparative effectiveness research, and that was obtaining information that would be directly actionable in designing health insurance benefits, where it would help avoid unnecessary care, promote best practices, or design networks and formularies that steer plan beneficiaries to optimal care.

Unfortunately, much of PCORI's publications have not been optimized for this use. Research with a focus on public health is also not optimized for use in design of employer sponsored insurance benefits.

Employers need information on the best care settings, the most appropriate treatments, the most effective prescription drugs. We need to know which treatments are likely to result not just in the best

health outcome but the least recovery time needed, the best restoration or maintenance of cognitive abilities to improve productivity, and the like.

We need information on both the direct and indirect burdens of disease, as well as what happens in patients with proper treatment. Undoubtedly, much of PCORI's work has touched on this, but in the eyes of the employer community, this is the gold standard. This is what we need in the realm of comparative effectiveness research.

I've also heard concerns from member companies regarding the populations on which PCORI's work is focused. Remember that employers' target population is primarily working families. That means that focusing on Medicare patients just doesn't really apply to us.

Issues like knee and hip replacement, Shingles, the interests of geriatricians, not that this work isn't valuable, we recognize the value, the problem is it doesn't generally coincide with the tens of millions or hundreds of millions of people who we provide benefits to.

Likewise, we know that PCORI does work of value that may not be directly relevant to employers or clinicians, such as, for instance, the best way to communicate with the hard to reach subpopulations, but because this work is not directly relevant to plan sponsors, they view PCORI's involvement with this as a missed opportunity with very limited resources.

I'd also like to mention that PCORI's work would be more meaningful if it was integrated at the point of care. Comparative effectiveness research needs to be included with live updates, clinical decision support tools, e-prescribing programs, electronic medical records.

In the 21st century, we cannot depend upon providers, plan sponsors, and patients to go to your Web site.

A little bit on PCORI's structure. None of this is meant to take away from the good work that PCORI does and has done. Employers are sensitive to the tens of millions of dollars provided, I believe about half of the funding, but we know some of this

is due simply to the way the ACA is structured and governs PCORI.

I'm sure none of you will be surprised to hear that ERIC members want and need cost effectiveness to be taken into account when conducting comparative effectiveness research, while we acknowledge that some patient groups have concerns about this, it serves neither plan sponsors nor patients to be kept in the dark. In fact, patients often have at least as much and sometimes more of a need to make informed decisions based on the cost of treatments.

When the time comes to address the future of comparative effectiveness research, I believe there is a consensus in the payer and plan sponsor community that cost effectiveness cannot be treated the same way it was in 2010.

Another problem is the political difficulty PCORI has in making certain tough calls on pharmaceuticals. As a large multi-stakeholder trade association, trust me, ERIC gets it. Being able to make those tough calls, to say that in a given

scenario, drug X is better than drug Y, period, that is the heart and soul of why we need comparative effectiveness research.

This is what keeps not just plan sponsors but also providers and especially patients up at night. We need PCORI's focus here, and we need your help. If changes are needed to make this possible, we are committed to pursuing them.

It is also critical to us that PCORI's hands not be tied. Whatever data is out there, whether public or private, proprietary or publicly funded, every bit of data must be at your disposal. We will fight to make that a reality.

The money collected in relation to PCORI, there remain serious questions as to whether such a significant portion of it should be directed to AHRQ, and whether they are spending that money wisely.

We want to ensure that PCORI is able to corroborate with other stakeholders to the greatest degree possible, whether that means partnering with specific research institutions or employer groups to

pursue issues of shared interest. We have to be able to leverage non-PCORI funds for the purposes that PCORI cares about.

I can't visit PCORI without mentioning that the structure of PCORI's Board is of concern to employers. Their members have expressed that there should be greater plan sponsor representation on the Board, and this in fact might help with some of the other issues I mentioned.

While we have the utmost respect for everyone here who sacrifices their time and their efforts to work towards success of PCORI, the current structure does not adequately represent the interests of those who are funding much of the institute's work.

In conclusion, nobody can say exactly what the future holds in 2019, whether there is broad agreement that comparative effectiveness research is still sorely needed, there is less consensus today on how that research should be conducted, obtained, and disseminated. We have an additional three years to observe and shape PCORI's work, and then it will

be time to reevaluate whether the current path is the right one to achieve the shared goals of both the proponents of health reform and the plan sponsors who insure most Americans.

I thank the Board of Governors for inviting me to participate in today's panel, and I look forward both to today's dialogue and working with all of you in the future to make sure that plan sponsors, providers, and patients have the information they need to make informed decisions. Thank you.

MR. BECKER: Thank you, James. Kathryn?

MS. WILBER: Thank you. I'm Kathryn Wilber. I am with the American Benefits Council where I work on health policy, and I'm primarily responsible for health regulations. Although I flew in from New Hampshire, I actually am based here in Washington. I happen to have been in Boston for some family visits and came in this morning to talk to you this afternoon from there.

I started my health care career 30 years ago as a certified nurse midwife in the Boston area.

I practiced in Boston, and then decided to follow a policy path rather than a clinician path.

I went to law school here in the area, and then went to work with what is now America's Health Insurance Plans, spent about a dozen years working on a variety of issues there, including what we used to call technology assessment, and then from there moved to the American Benefits Council, where I have been for about 10 years, working with large employers, many of the same or similar types of companies that James referred to.

They are sponsors of employee health benefits programs that cover not only their employees, active, but also retirees, and spouses and dependents.

As mentioned, our plans are generally at least 10,000 employees. We do have plans that are covering a million covered lives. That is a big investment or it will be seen that way, it is being seen that way.

I'm giving you this background to sort of explain why as personally and professionally I am a

champion of comparative effectiveness research. The question, too, is why do employers self-insure, and the reason typically for a larger employer is because it gives them the flexibility to tailor the benefit coverage to the needs of the workforce.

If you have a workforce that is in manufacturing or in trucking, you might have to focus on musculoskeletal issues, chronic disease, those kinds of things, versus perhaps retail where there is a younger population, maybe your concern has more to do with maternity care and pediatric issues.

You have a flexibility to do that when you self-insure. You're not just pulling an insured product off the shelf.

Under the ACA, which has taken up almost all of our time since its enactment and its implementation, as a large employer who self-insures are not subject to the essential health benefits package, which is what the insured market and the qualified health plans are supposed to offer.

Again, flexibility. I think a recognition

by Congress that large employers could have that room to continue to do what they do, to design and implement their coverage, their benefits, and they do use again, the insurers, the carriers, to administer those benefits.

Again, I just wanted to make sure that we were clear about where our perspective is coming from.

Again, support for comparative effectiveness research, you might remember, too, that as part of the ACA, there was a transition reinsurance program fee that created quite a lot of controversy for employers. It was a contribution to the whole risk reinsurance program. A lot of opposition, I will tell you, among employers for that fee.

We did not hear that for the PCORI fee. Clearly, it's a little smaller, quite a bit smaller, in fact, but I think that was a reflection of sort of recognition there is value here that they weren't seeing for the TRP fee.

Again, value of comparative effectiveness

research for a number of reasons. One, we want to know what works and what doesn't work. This is about quality. It's about preventing the dissemination of treatments that don't work. I think this audience knows that better than we do, even what does that mean.

Once you start covering something, it is awfully hard to pull that back, and if we don't have strong evidence, it is worrisome.

I have also been working on mental health parity issues with the Departments of Labor, HHS, and Treasury. I spoke in a listening session to the Parity Taskforce about two months ago, and one of the articles that I cited was from the New York Times this fall about residential treatment for eating disorders, and quotes a dad that said I spent $350,000 for something that was ineffectual, and that the standards just aren't there for that sort of treatment. We are all struggling with this.

This is very timely, and it continues to be. We are also, I think, clearly moving or moving, we are there, in terms of investing in and

understanding how to best implement a value-based insurance design. How do you get there, and the way you get there is having the best information around effectiveness.

We are now several years into the institute, very much appreciated the outreach from staff for the Board, and one of the things we talked about is just to help us understand what the research agenda looks like, what is the status of the research projects, where do we have results, what is ongoing, what is on the drawing board. I think some fairly basic questions.

We ask that because that is kind of basic information that the employer community is going to want to understand when they look at sending in $2 million here or less yearly, help us understand what is the status of the projects. They are going to want to know how is this relevant to my coverage, my benefits designs, or not. I think that is just the first question.

Once we have that, then how do you communicate that in a way that is accessible and

usable to this particular constituency. We recognize you have a range of constituents here for this information.

Doing so in ways that gets to an audience that is not steeped in science, but does understand, I think, coverage policy and evidence, where there is evidence and where there is not. Putting it into a form that makes it understandable and accessible to employers, to large employers.

They work with really fairly sophisticated people, but those are the kinds of questions that we are going to be getting, particularly a question of should this continue. Do we think it should continue, are we going to support reauthorization?

The kinds of topics that I know you have had input from clinicians, from the insurance, third party carriers, et cetera, I will mention them briefly, but they wouldn't be any surprise. I mentioned mental health, chronic disease. I think the number out there is still about the same, about 20 percent of the population accounts for 80 percent of the costs, and more and more employers are really

trying to look at those high dollar claims and understand how do we get control there of that. Autism comes up frequently as well, so understanding how those therapies work or don't work is an ongoing area of interest.

I guess I'll end with a message of what's the data and how do can you put it in a format that is going to be understandable and accessible and meaningful to an employer audience.

I want to say we empathize a bit with that because under the ACA, group health plans are under a similar obligation, and we were directed to create documents to allow comparison of benefits coverage, and the insurers had to do the same thing, reading levels, et cetera, a couple of pages, and it's not easy. We get that. It's important. We have been working to do something similar to make sure that we are able to put information into the hands of the ultimate user, for us, again it is the participants and employers.

I will end on sort of what do I hear about most. We travel around the country and talk to

employers in every major metropolitan area, both coasts, et cetera, and all industries. The oil and gas industry right now is very different from the tech industry. You have zero unemployment in the tech industry, you have a down market in oil and gas, so they are looking at benefits a little bit differently in terms of where they make best use of their dollars. One is working hard to recruit and the other is not exactly in that position.

The single common thread is we are desperate to engage our employees, our participants, and especially our spouses who cost more than anybody in a plan, in the best way possible. Looking for ways to use effective communication is a challenge for all of us going forward.

MR. BECKER: Thank you very much. Ted, bring us home.

MR. CHEATHAM: Are you saving the best for last? Just kidding. I apologize profusely for not being able to get there, I tried very hard to make it there, because it is so much better to be in person, to be able to see each other, and see what

we are doing.

I want to say wow. I think James and Kathryn hit this, you almost don't need me. I think James said it much more eloquently than I did, and Kathryn probably has a better grasp of that. I won't bore you.

I just want to say I echo their comments, and I want to give you a couple of examples to maybe understand how we do this as a small little state payer, and understand the politics that we have as a health plan in a state, because my boss is elected. When any of our constituents don't get what they want, they write a letter or call the Governor, and we are a very small state, and everybody knows the Governor. That's how he got elected. It does bring the politics into this that we need help for as payers, much like both James and Kathryn have said.

Some examples. Let's look at programs for prostate cancer. There is a drug that came out that cost $90,000, extended life by four months, and we have to ask the question -- I agree with you, if it is not four months, it makes a big difference, and

if that four months helps me get to see my child graduate from high school, those things are very important to unique people.

We are setting policy at a state level that maybe there can be exceptions for, but we need a policy rule and we need some help. I say things very crassly and very bluntly, so please, since I'm not there, just try to understand the message I'm trying to convey, not the way I'm conveying it.

I really do think it is time to throw into this mix a little bit of the efficacy of the time life value of the expenses that we are making. Think about this for just a minute.

The Affordable Care Act took us into that mode where most plans in the states, including ours, had $1 million lifetime maximum. That went away with the Affordable Care Act, for good and for bad, and it is great for the end consumer, it is bad for the health plan.

I'm not taking a side here, it is just in the old days when somebody would go into the hospital and start to reach that $1 million maximum,

those hospitals realized benefits were going to start to decay, and they had to get a mitigation strategy for that patient.

That mitigation strategy I'm seeing is no longer there. It is looking like an unlimited pocketbook. I have people sitting in a hospital that are going to die in a hospital at 3 and $4 million, where it used to be $1 million.

What I'm telling you is as a health system, I can't afford this, and I need help at a level of credibility, at a national level, which is PCORI, who has that respect and integrity, to say this is not appropriate. I want you to go a little farther.

In the past, I've looked at PCORI, on the prostate cancer issue, for example, PCORI does a great job of saying look, here's what you can do with Da Vinci surgery, here is what you can do with wait and see, here is what you can do with the insert pill, there is the four or five treatments and what all the impacts are, but you don't go far enough to say you really shouldn't be covering this because you're not getting efficacy out of it.

We want some guidelines that we can set policy from, much like James said. PSA screening, for example. It is now recommended not to be done except in cases of special risk factors, but just the other day in the Kaiser News Bulletin, there is a physician advocating that was a wrong decision, we have to continue to do PSAs. I don't know the answer. I'm not a physician. I want PCORI to help me with those types of things.

New technologies coming out all the time. We have the push on for colonoscopies, right, for 2020. There is a big push, our Governor signed a pledge to get there, increase colon screening. That is all well and good, but now we have three or four fecal occult blood tests out there with varying pieces of efficacy that cost money, present false/positives or false/negatives, and require retesting of a colonoscopy anyway.

Those are the things to help me. I want to give you one final example, and I will stop and take some questions. Rheumatoid arthritis, as you all know, is a very expensive disease with a very

expensive medication, in the thousands of dollars. There was a study that showed a triple cocktail of generics and lower cost preferred brand drugs could accomplish the same thing with the same outcomes. For the life of us, we cannot get a rheumatologist in this state to adopt those guidelines no matter how hard we try.

I understand three pills is harder to take than one, and taking some at morning and some at night is harder than taking them once a day. I do understand those things.

When you can do something for thousands and thousands of dollars less that is just as effective, we have to find a way -- you have to help us push that as a guideline. It's like new drugs. If I understand it, the FDA approves drugs just to prove that they don't kill anybody, not that they are going to be much better than what is already out there. We need to take a hard look at those as well.

I will stop there and take questions, and I hope I wasn't too crass.

MR. BECKER: Thanks very much.

DR. NORQUIST: Larry, I'll let you recognize people.

DR. JESSE: All this discussion about value has inherent conflicts. Sorry, Bob Jesse, Board. The equation we use is value is quality over cost, quality is in the eye of the beholder, and cost is not always in dollars. If you're looking at it from an insurer's perspective, it is a very different view than if you're looking at it from a patient's perspective.

Kathryn, you are in a sort of interesting position because as an employer, if the insurance company denies, you can be an advocate, but as the employer and the insurer and you issue a denial, then it creates a different level of conflict with the employee base.

One of the hopes, I think, of PCORI is we can deconflict that by providing the right kinds of evidence that both patients, because that is who we fundamentally represent, as well as employers and insurers and everybody else, can begin to make the

kinds of decisions that need to be made, but we can do it by communicating information in ways that everybody understands it, so there is not the misunderstanding of why denials, for instance, are made.

If there are different ways PCORI should be operating, I'd love to hear that from you all.

MS. WILBER: I think we would agree with your comments. First of all, as you know, there is a process where there are benefit denials, whether it is made by the TPA and then ultimately by an employer, which retains the ability to do so, and that is through an ERISA governed claims and appeal process. That includes external review, and third party review is as a result of the ACA. Many employers were doing that anyway, especially for this very hard call cases.

That is where the kind of information that PCORI can provide is very helpful. I completely agree with that. I think what we are also talking about is how do we translate or communicate that information in a way that people understand what it

is and the value of it, what does it mean for me as a patient or as an employer making coverage design, and for administrators making a decision under those plan terms as to whether that is covered under the plan, but then is it medically necessary for that particular patient at that point in time. That is where it really comes down to specifics.

MR. BECKER: Alicia?

DR. FERNANDEZ: Thank you. Alicia Fernandez, I'm a Professor of Medicine at UCSF, and I'm sorry to say I do work with those hard to reach populations.

I really want to thank all three of you for your directness and your honesty. I find it extremely useful and helpful as we move forward.

Let me be equally direct and honest. You don't want a research institute, you want NICE. NICE is a British institute in which evidence is brought together and a clear direct guideline is issued. That is not what PCORI was set up to do, not only because it was told not to take into account costs, and I agree with you that it should

take into account costs, but it wasn't set up to say don't use that prostate drug that extends life by three months. It was set up to say does that prostate drug extend life, and is it better than this other prostate drug that extends life.

If you want clarity and help on making the hard call, I suggest you make the hard call and say we will not cover that prostate drug, it is not going to be part of what we do, or if that's not within what is possible, I wonder whether what you want is not a somewhat better PCORI, but what you want is not a research institute at all, but rather a place where these very difficult, very appropriate national conversations can happen.

The reason I think this is worth stressing is that I think you may be criticizing PCORI for not doing what it never set out to do. I think it's fair to criticize PCORI for not doing well things it may have been set out to do, but not so fair to criticize it for not being able to play a central national role that it was not set up to do.

I think having that distinction clearer in

your minds will help us work better together as we move forward to look at PCORI's reauthorization, and as we all think what should PCORI 2.0 be like, or whether there should be some other form of organization or some other real different metamorphosis of PCORI.

Anyway, thank you very much for your input.

MR. CHEATHAM: If I may, I agree with you 100 percent, and I said please try to understand the message that is there. Gray and I have had this conversation many times, that really is not what PCORI was set up for. I agree with you. That was not the charter. I think some of the things we are looking for was clearly not in your charter.

There is clearly a role for an unbiased research institute to help us determine the science for this, and I think you asked where is PCORI 2.0. I don't know how we link you into things like the Oregon Med Project and some other comparative effectiveness research organizations so you can give us the unbiased science, and we can have the dialogue that you are talking about on how to

implement that science effectively.

MR. BECKER: Kathryn?

MS. WILBER: I agree with your message and Ted's comments as well. I think we understand that what PCORI was authorized to do by Congress is not NICE. I didn't quite mean it that way.

I think I'm at a very basic level with what I'm hoping to communicate to you, tell us what you have done in terms of the research agenda that you have taken on, that you have funded, and what is the status of those projects, where are the results, what are you studying, when are we going to get the results of what is in the pipeline, just really basic information that in your world, I think, you are able to talk the talk as researchers in clinical practice.

It's very important that information also be made available to these other constituencies, and we are one, and individual patients, too. If I'm having trouble looking at your Web sites and understanding what you are delivering on, how does the average American?

This Administration has been remarkable for transparency and imposing requirements of transparency. We now have average ordinary Americans who comment on regulations. In the old days, you needed the Federal Register to do that, and you needed to understand the process. Right now, you can go online and people are.

I can help my members distinguish NICE from your mission, but that might be something you might need to do as well in terms of saying hey, this is where we have jurisdiction and this is not. Maybe that is needed, but it is not something we can do.

MR. GELFAND: I also agree with you. I will say this, like many parts of the ACA, the authorizing language that created PCORI was an experiment, and we have now had some years to look back and say, well, did we really design it to get what we wanted and what we need, or are there some changes that may need to be made.

The way I'm looking at this conversation is a forward looking one, it is not about wagging a finger at folks for what they did or how they did

it, but to say this is what we need, and we have always known exactly what we need. We need information we can act upon. Going forward, our goal is going to be to ensure that PCORI has the ability to get that information and the incentive to make that a priority.

MR. BECKER: Sharon, Ellen, Joe. Sharon?

DR. LEVINE: First of all, thank all three of you for your time. We feel your pain, actually. For six years now, it has been very clear to us that the mandate or the chartering of PCORI was designed to produce exactly what it is producing, and that was based on lack of agreement. It was fundamental and widespread lack of agreement about purpose and what we had was the result of negotiation and compromise.

Our job has been for the last six years to do the very best we can in terms of, as Felicia said, executing with skill and as much speed as we can on the charter we have.

I think the good news and the bad news for self-insured employers is that if everything was

fully insured, you would have no choice. There would be no choice. You would be forced to cover everything that is under the ACA. That's the good news. The bad news is you have a choice.

This is just my personal opinion. The level of detailed information required to make benefit decisions about interventions is very different than the kind of information, which is largely about probabilities, to make informed clinical decisions with good decision support.

The easy ones for benefits, it always works or it never works. Those are easy and straightforward, and a very small percentage of what we deal with in clinical care. I think the issue for the FDA that Ted mentioned, I think it is probably a little bit of exaggeration, but it is comparing an intervention to placebo, the vast majority of the time.

Our job is to pick up from there and say what can we add to the understanding for whom this might work and under what circumstances. It's very different than saying we will cover something or we

won't cover something. You end up with the burden, the choice, the opportunity, if you will, to say we need information about under what circumstances we can with confidence approve coverage, that it won't deliver us from value or deny it with some understanding there is science behind the denial.

The application of that to the individual is a tricky business. As I said, we feel your pain. I think we are all committed to trying to produce as much information and evidence, to the extent we can at the coverage level, but perhaps equally important, at the clinician/patient/family level, to think about the implications of the choices you have. None of our jobs are easy.

MR. BECKER: Ellen?

DR. SIGAL: First of all, let me apologize because I was out of the room on an urgent call, but I think I have the gist of what you are saying. I just want to say the complexity -- I work very closely with FDA and work with patients on personalized medicine.

You are making an assumption that we have

the science, that we absolutely know what is going to work for a particular patient, and the answer is it's evolving and we don't know. If you have a very clear biomarker and you have a drug that works, it's pretty easy. Even in immunology today, we are so excited, it fails 80 percent of the patients.

It is hard to know, depending on the trials, if the essay was accurate, is it FDA approved, is it not, the drug didn't work for the patients. You are asking us, which is not our mandate, but you are making the assumption that the science is there and we know the answers. The answer is we don't, we're trying to work on that.

Having said this is a very confusing time, because right now I'm dealing with where patients want access to all these protocols, and we are trying to do that with single patient now with the FDA, we are doing a pilot in cancer. It is very complicated because when a patient has a diagnosis, a very ominous diagnosis, particularly where there are no treatments, they want access to those drugs.

It is very hard on an individual basis to

figure out what is right for that individual patient and what is right for society. What I think people are saying is that we actually know the answers, and the answer is we don't. We are getting there, and we are getting a lot better as we have more biomarkers, we have targets and clinical trials, it is going to be easier, but I can tell you today, you can go to three different cancer centers for the same disease and get three different options. Why is it?

MS. WILBER: Again, I think we probably have more common ground than we realized or understand because that same patient is coming to the employer, too, and saying I want to go here, I want to go there, and struggling with that as well.

MR. BECKER: Joe? Ted?

MR. CHEATHAM: A comment on the cancer, if you don't mind.

MR. BECKER: Go ahead, Ted.

MR. CHEATHAM: I'm sorry I'm not there. I will try to give you another interesting example that goes to your science question, it's very

unique.

Marshall University in West Virginia has developed a program called ChemoID, and they have proven great effectiveness on two or three cancers, one of them is a rather rare brain tumor, and they will then take a biopsy sample, run it against 20 or 30 known treating drugs, and can then provide the physician with the course of treatment that will prove most effective, scientifically most effective.

They found 80 t0 90 percent of the time the drugs recommended response, so we are doing a pilot with them now, and it has been extremely difficult to do a pilot because you will go to a doctor, and we are doing it, but we are doing it with a closed set of physicians that have accepted the science, but most of the cancer treating physicians in the State of West Virginia are going I don't care if that Chemo ID comes back and says use drug A, I've been treating my patients with drug B for years, it's the standard of care, I'm not going to stop.

What happens is you put the person on drug B, 80 percent of them fail. They have been on an

expensive drug that we paid for, the patient has suffered, and you know cancer is very painful to treat for the patient, and then the patient has to start a new regimen back to drug A, which we said they should have started in the first place.

The adoption is difficult. I understand your side, but politically, us having something at the Federal level to help us say this is good science to help change is acceptable, because it is very difficult for us to change in the state. I hope that makes sense.

MR. BECKER: Ellen?

DR. SIGAL: Because I work a lot in this area, I would like to say if they have an assay that works, let them publish, and let them get FDA approval of it, and let them go in a peer review journal. Everybody says that they have something that works, and we don't know if it works.

It's hard to ascertain whether that is valid or not valid, whether an assay is really giving the response they claim it is, let them publish it. Let them work with FDA on it. If you

get that, then in fact people will pay for and people will pay attention to it.

MR. CHEATHAM: Agreed, and that is what they are doing now. That's exactly what they are doing now. I agree. Point taken.

MR. BECKER: Joe?

DR. SELBY: Thanks. Thanks to all three of you. I really want to add my gratitude and appreciation. What you are saying isn't surprising to us, but each time somebody says it, they put it in a slightly different way, so it's helpful. It does sink in.

We have signaled our strong interest in getting to these products in short order, and held a meeting, I think James, you were there, a couple of weeks ago on the 14th. We heard about the types of products that would be helpful.

I want to say two things. Number one, I'd like to round out a comment that Alicia made about NICE. I would amend what she said, that actually what we all need NICE, to what we all need is a combination of a NICE-like entity and a PCORI-like

entity, and in fact, that is just what they have in the U.K. They have the NIHR in the U.K., which is our sort of sister agency in the U.K., except they have been in existence for about 20 years. They are now producing things like the very nice study of patient-centered and long term outcomes in prostate cancer in the New England Journal a couple of weeks back.

They worked very closely with NICE in determining the information needs that policy makers have, and the evidence gaps, and handing off the information when they do produce it to the policy makers.

We are still looking for a relationship like that in the U.S., and I think going forward, one of the things we have learned is that getting to just the right question is not easy. The question that really will settle the policy makers, the clinicians, the patients' decision-making needs. You can't escape the fact that you have to be in close contact.

I hope these next three years, as somebody

pointed out, are years of greater contact, where we talk both about what we can do now and perhaps what our next generation, as somebody said, pure science, I think we are applied science, entity could contribute.

There is a need for somebody who takes this information, perhaps it could be PCORI, but there is also some real virtue in separating the producers of the science from those who try to digest it and make policies.

MR. GELFAND: I just want to quickly go on record saying we are not in favor of a panel of government bureaucrats who will decide who and who cannot get which treatments when or for how much. That is not what we are pushing for.

DR. FERNANDEZ: Can you explain what you are in favor of? You are asking for something similar to NICE. It would be fantastic to partner with you on this. What would you be in favor of? Who should be making that call?

MR. GELFAND: Plan sponsors should be making the calls for what their plan will pay for

and sponsor. They should have information that they can use to make educated decisions about what they will and will not include.

Whereas, when I picture NICE, I picture them making decrees such as once you are over 74 years old, you may not get a hip replacement, right? We have no interest in something like that. What we would like to know, for instance, on the cancer drug that extends life for only four months and costs hundreds of thousands of dollars, what is the quality of life of those four months?

Are there other treatments that could better suit the needs of specific individuals? Does it make sense to increase the premium for the other 999,000 people who are covered by our plans in order to pay for the one person who is going to need that particular drug?

Those are the kinds of questions we are asking when we are presented with this information. That is what we are hoping that a group like PCORI can produce, information we can use to make informed decisions about that.

MR. BECKER: Bob?

DR. ZWOLAK: Bob Zwolak. I'd like to add my thanks to you for coming and sharing your comments. I think it is clear we don't like coverage policies, and there are certainly many things that we don't do, but what we should do and can probably do better is comparative effectiveness research.

I wonder if I could put you three on the spot, if you're willing, to say what are your two or maybe three very specific highest priorities that just jump out of your mouth, research projects in comparative research that PCORI could potentially sponsor.

MR. GELFAND: I have one that's been burning in my brain for the last half hour, so out with it. There is legislation that is currently moving through Congress that would add eating disorders to mental health parity requirements, which means my plan sponsors are going to be required to cover the inpatient stays for a month or longer for eating disorders.

We need data on whether or not those are effective treatments. We badly, badly need data, because it is insanely expensive. As I said, for the group of people who that helps, that may be good, but we are going to be talking about hundreds of thousands of people who are going to be paying more for their health insurance in order to pay for that. We badly need to know what works and what doesn't work in that specific space of mental health.

MR. CHEATHAM: You know, James mentioned this earlier. In our plan, specialty medications are going up at 25 percent a year. Some generics are doing the same. You have all been reading about all these issues with drug pricing and what manufacturers are doing.

It would be extremely helpful to look at the efficacy of some of those drugs across the board.

DR. NORQUIST: Larry? I think Leah has the final, and then we are going to need to stop, we are about out of time.

MR. BECKER: Kathryn can give her example.

MS. WILBER: Which is essentially seconding, I think clearly drug issues are rising very, very quickly to the top of the heap for all constituents. I also mentioned the mental health challenges, eating disorders was one. That is certainly not the only.

If you were to look at buckets of issues that employers are really grappling with now around decisions and what's the best thing to cover and why, those are two areas.

DR. NORQUIST: What I would say is you are certainly in an area that could use some evidence. It's interesting you bring that up. Many years ago when I was at the NIMH and we were doing clinical trials, residential treatment of children for a variety of mental health things was one of the number one issues next to the cost of the new antipsychotics at that time. It remains an issue, and I would say surely it is something someone should put some effort into.

The other thing I was going to say you did

mention. One of the things we get pushed a lot to do is to really do trials on the new high cost drugs, but when you look at the costs, certainly as an employer, many of your biggest costs are not about the new -- maybe one new blockbuster drug, but often they are the common, if you will, treatments, that go on for a long time that are really costing you a lot.

If you were going to weight in some direction --we only have $500 million a year, so it's not like we get to do all of these trials, but if you were going to weight where you had to put your effort initially, would you go for the new big blockbuster high cost or would you really focus on some of these, as you said, chronic illness issues?

MS. WILBER: I think our vote would be more on the latter. Again, musculoskeletal, joint replacements, chronic low back pain, garden variety of complaints that people have that we still have some uncertainty about what works best.

DR. NORQUIST: One of the things I see quite often is pain, tons of different kinds of

treatments, and of course, the big issue is insomnia, and the kinds of interventions and stuff that are put into that.

MR. BECKER: I want to thank you three for coming. Ted, thank you for being on the phone.

DR. NORQUIST: James?

MR. GELFAND: I was just going to agree with that. I think the drug companies are moving away from focus on blockbuster to focusing instead on target populations that will be on maintenance and medications for the rest of their lives, so that is where we want to focus, too.

DR. NORQUIST: That's very helpful. I think what we are saying is there is an opportunity to try to do something together. We can all get the kind of information that we all want.

Thank you, Larry, for putting this together. I want to thank you, and thank you, Ted, for also being on the phone.

MR. BECKER: Thank you for being so candid.

[Applause.]

MR. CHEATHAM: Thank you for having us.

DR. NORQUIST: We are transitioning here with Lori Frank and Laura Forsythe.

DR. SELBY: As Lori and Laura move to their seats at the table, I just want to say this is an exciting presentation for me because a couple of years ago, Harlan Krumholz made a strong point about beginning to use our own data to understand what we are doing. One of the most important things I think we are going to be called on to do in 2017, 2018, and 2019, as people think about our renewal, the question of our renewal, is whether all this jazz about engagement really makes a difference.

The presentation today is a database beginning to exploring a question that we have to answer fairly soon, and that is about whether our engagement investments -- what are they reaping in the projects, and how might we look at these data in ways that would help us distinguish whether they are making a difference.

Thank you very much.

DR. FRANK: Thanks for that, Joe. I'm Lori Frank. I'm Program Director for Evaluation and

Analysis, and I am joined by my colleague, Laura Forsythe, Associate Director.

We're very excited to be here this afternoon to share with you very briefly some information that we shared in greater detail with the evaluation strategy working group that includes Board members and Methodology Committee members earlier this month.

In the interest of time, we are moving very quickly through these particular results, but we want to be sure to leave some time for discussion of the direction of our future work in the area of understanding the impact of engagement in research should take.

Today, we are focusing on two questions. How active is engagement in PCORI projects? Does engagement in research lead to changes in study designs, study questions, study processes, or in the outcomes that are chosen?

As part of this particular presentation, we are updating from the last time we spoke with the full Board, which was about 18 months ago, and we

are excited to say we have much more data than we did then, so at that point, we just had information from projects that were completing year one, now we have information from projects completing years one and two, and we have more data.

When last we spoke with you about this, we were relying on data from individuals who agreed to answer our questions, awardees, now we have comprehensive data from all awardees, which to us makes this information much more powerful.

We also have always presented to you the signals that we are finding qualitatively. We have talked today already earlier about some of the examples that you hear from awardees about the impacts of engagement.

Those examples can be very, very powerful, but we are particularly pleased that we now have enough qualitative data that we were able to complete a robust and systematic qualitative analysis, so it is another way to enhance what we are learning. It compliments what we hear through the quantitative data that we are collecting, and it

allows us to hear the voices of the awardees and their research partners in a different and we think a very powerful way.

To orient ourselves, this is the logic model that we are using as our evaluation framework with inputs on the left to outputs on the right. We are working from the assumption that there are unique elements to the PCORI Way, including the way in which PCORI goes about topic capture and prioritizing the research that it funds. Definitely unique ways PCORI is approaching merit review, et cetera.

The logic model flows through that next green box, which is where we are funding patient-centered CER using this unique PCORI Way. Patient-centered CER is a function of engagement, and performing the research to high methodologic standards.

Together, that patient-centered CER box leads to an output, which is the goals we have all set for ourselves at PCORI, to increase the quantity and quality of useful information, to speed the

uptick and use of that information, and to influence the way that others conduct research.

The ultimate goals are always there to the right. In the purple shaded boxes, we believe those goals will lead to better health decisions, improving health care, and ultimately improving health outcomes.

I wanted to set that context because we are zooming in now on that green box, where we have patient-centered CER. This is where we are examining engagement in research more closely.

On the left, you see real descriptive variables, the who, what, when, why, and how of engagement. In that center light shaded green box are the research questions that we have about the ways in which engagement is making a difference. We are positing that engagement in research changes the research questions, the study designs, aspects of the study process, and the outcomes that are chosen.

It also changes the ways in which the participants experience the research which leads to positive effects on recruitment and retention and

rates of study completion.

As a group, these variables can describe study quality which is one output to get us toward our goals. We are also saying that engagement in research changes to whom and how the results are disseminated. It improves trust in the information, and it enhances understanding of the information that derives from the research that is patient-centered. That, too, is leading us to those outputs on the right.

We are thinking of this as our predictive variables on the left with intermediate outcomes there in the center, ultimately pointing towards longer term outcomes, and to make this concrete, we have put some time notations with this.

We have been collecting information, as you know, from our awardees and research partners, since PCORI has started to fund projects. We now are amassing a reasonable amount of descriptive information, and through this past year, we have been able to collect some information on our intermediate outcomes.

We are turning our attention now to using those data to help explain that relationship between the predictors and the intermediate outcomes, and that is some of what we will describe today, how we are headed in that direction.

Those longer term outcomes will be able to be addressed through the information that we are collecting in the out years, 2018 and 2019.

Another way to frame this is when can PCORI answer the key questions we all have about engagement in research. We have begun to do so. We do have information and we will be sharing some of it now. As I said, we shared some fairly detailed information with the evaluation strategy work group.

We are moving from that description to explanation. What you see as time is moving on is that we are able to explain relationships once we have enough data.

Let’s turn to the information that we have. This is our tree of knowledge for engagement in research. Starting at the bottom, the lower left, we are always monitoring what is going on in the

literature, and we are really pleased to see more and more awardees reporting out.

In this case, our focus is on what they are reporting out about their engagement and what they have learned. We have a nice example to share with you in just a few minutes.

On the lower right, it is just a reminder that PCORI is actually funding work on understanding engagement in research, and obviously, we are doing what we can to harvest that information, so beginning with pilot projects that has this as an aim. We also had a section of the Improving Methods portfolio focused just on this, and we funded some engagement awards on this.

That next level up shows pipeline to proposal awards where we are also taking the opportunity to learn about the engagement that is happening in those projects, and we have reported back to you on some of our stakeholder views work, where both formally and informally we have been speaking to a range of different stakeholder groups about a range of issues. We do take those

opportunities to ask them about their knowledge of and attitudes toward engagement in research.

The focus for today is on those top branches, what we hear directly from our own research awardees and from their research partners.

As part of this update, I wanted to share with you how we are going about collecting all this information. At annual intervals, we have the awardees report back to us. We are now hearing from all awardees. The last time we spoke, it was just those awardees who chose to answer the questions. The awardees nominate research partners for us to speak to as well.

For the awardees, we hear through our interim progress reports. We have over 250 projects represented now. We have heard from over 250 partners through our Ways of Engaging ENgagement ACtivity Tool [WE-ENACT].

I wanted to make sure to be clear that there is not a one-to-one correspondence here, so the research teams can nominate more than one research partner for us to follow up with, and in

fact, about two partners per project are represented here.

We ask about both open and closed-ended items, and that is why we are approaching this with both a quantitative analysis of the data and a qualitative analysis. We are appreciative of colleagues at RTI who have been helping our own internal staff on some of the quantitative analysis, and very excited to share what we are learning out of cluster analysis, specifically, as it is posing us to move from description to explanation.

We are also working with external partners who have expertise in qualitative analysis to supplement what our own internal staff brings in terms of that expertise.

American Institutes for Research and Research Talk have both been instrumental in aiding with these analyses. Together, we have developed a codebook that is hierarchical or multi-level, where we have identified themes across all of these awardees. I really want to stress how exciting it is to have all of these data now for this

qualitative analysis.

Because we have so much data, we can document essentially how prevalent these themes are across all the awardees. We are really moving from the early detection of signal that we have talked to you about before and that we all see in case reports, to a more conclusive documentation of learning out of the qualitative data.

The first question is how active is engagement in PCORI projects? I want to remind you that PCORI does require meaningful engagement in the work it funds, and we assume that means that our projects will have more stakeholder communities represented, and more active involvement than has been historically seen.

What do we see when we take a look at the data? First, the data aren't mutually exclusive. There are multiple stakeholder types engaged per project. In fact, our awardees tend to engage between four and five different stakeholder communities in their work.

Clinicians and patients top the list. We

see a fair representation from advocacy organizations and from health systems. About half of the projects are engaging caregivers in some way.

I will just call your attention to that third bar from the bottom, that is the payer bar. The last time we spoke, remember that was a year and a half ago, with much less data, about 7 percent of our awardees reported they were engaging with payers, and that has increased as the projects have matured, and as more projects have come on line.

In what ways are these stakeholders engaged? Beginning at the top, our awardees are reporting to us their stakeholders are engaged as research team members. We think this is a very active form of engagement, and in fact, 44 percent of the projects are telling us that not only are they research team members, they are actually co-investigators. We find this to be quite striking.

Eighty-one percent of the awardees are also telling us they are engaging stakeholders through advisory groups. Also, an active form of engagement, but different from being a research team

member. Generally, these are advisory panels where they convene multiple times through the course of the project and provide input.

At the bottom, we have a less active form of engagement that is reported to us, where partners are surveyed or sent polls or interviewed. Again, these data aren't mutually exclusive, so there are multiple ways in which our awardees are engaging the communities that are their research partners. In fact, we find with 75 percent of our projects, they are using two or more of these approaches in their projects.

When in the course of research are these partners engaged. We are right centered here because we have year one and year two data so far. We look forward to being able to report back on the later stages, including all the way through to dissemination, but we have cut it here at data collection.

You can see there is active engagement of research partners in deciding even what the study is about, choosing interventions or comparators, and in

three-quarters of the projects, they are helping to choose the outcomes that are studied.

I briefly mentioned that we had completed some cluster analyses. We haven't updated. We have always been focused on using our descriptive data to begin to understand different models or topologies of engagement.

The team has looked in a number of different ways at what would form a cluster, what factors lead to differential models of engagement. We found that the number of partner types engaged, the number of approaches, and the number of phases of engagement together help us to differentiate meaningful models of engagement.

There are roughly three levels. We labeled the top level "intensive." We have an intermediate level. That third level is called "limited." A really important point is this is limited relative to other PCORI projects.

If you think about it relative to projects coming out of other funders, it's not limited at all, it is quite a bit of active engagement. On our

scale, we have these three topologies which ultimately we can put into service moving toward explanatory models.

With that, I will turn it over to Laura.

DR. FORSYTHE: Thank you. We are also interested in understanding our awardees' views on the extent to which their partners influence each phase of the projects they are involved in, and we see notable consistency across the phases of the projects shown on this slide, such that at least three-quarters of the awardees report their partners had a moderate or a great deal of influence on each of these phases.

These ratings are helpful to us in setting up future comparisons of interest because we can look at those projects that reported none or a small amount of influence compared to those reporting a great deal as we try to understand differences in both their approaches to engagement and the effects of engagement on their projects.

When we compare what we are learning from PCORI projects to what is documented in the

literature, including in recent systematic reviews, we see PCORI projects do display a substantial amount of engagement with multiple partner types engaged across multiple phases of the project, and through multiple approaches, and our awardees believe that their partners are having a meaningful influence across all the relevant phases.

This is good news, that across the PCORI portfolio, our awardees are reporting engagement that is consistent with our expectations.

For the question we turn to next that we want to begin to answer today relates to the effects of that active engagement on the study questions, design, processes, and outcomes. PCORI expects engagement will affect key aspects of the project in meaningful ways, although the specific effects that we would anticipate would depend really on the project content and context.

To look at this more closely, we turn to our qualitative analysis. The reason is because those open-ended data provide a much richer description of the ways in which engagement is

making a difference than we can learn about through quantitative or close-ended questions.

As Lori mentioned, we have a relatively large sample, over 250 awardees and partners who have provided this open-ended data, and those data went through a robust qualitative analysis process on multiple aspects of the project.

Today, we are focusing on the project processes and the impact of the partners on the projects. We can also look closely to understand how awardees' perceptions and partner perceptions compare.

With regards to what difference engagement is making in their projects, we actually see notable consistency in the themes identified from both awardee responses and partner responses. Everything reported on this slide today is a theme that was documented in at least 10 percent of both awardee and partner responses, although most of them are much more common than that.

We hear from both awardees and partners that engagement was making a meaningful difference

in terms of selecting the research question, selecting the interventions and comparators, choosing which outcomes will be measured and how they will be measured, developing a data collection process, including when, where, and how the information is collected. The strategies for recruiting and retaining participants.

Also, both groups highlighted the importance of engagement toward enhanced enrollment rates in their studies.

One unique thing we heard from the partners was that they feel like research teams have a better understanding of their perspectives due to their involvement in the project, and that they better understand their experiences, experiencing or managing a given condition or their priorities for where to go with the treatment.

One thing I want to note about these themes is it is very exciting to see what we are learning and a reminder that we are hearing from projects in their first or second year, so we expect this list of the ways in which engagement is making a

difference to grow as the projects progress towards completion.

I want to give you one illustrative example to help make these themes come to life a little bit. The example here refers to the themes we told you about with regards to selecting a strategy for recruitment and enhancing recruitment rates.

For this particular project, a caregiver partner told us about the role that the partners played in revising their recruitment strategy, and they noted they helped discuss with the project team how to make families feel more at ease, why families might choose to withdraw from a study, and better ways to communicate with families who are already involved in the studies. This partner told us that as a result of that, more families stayed in their study.

In the project reporting, the awardee team told us based on what they heard from their partners, they knew they needed a recruitment strategy that was more responsive to busy families' needs, and they wanted to change their recruitment

message to ensure that potential participants knew that the study was designed with families, with the intent of improving communication with their physicians.

What the awardees told us is after they made the changes to their recruitment strategy, discussed with their partners, their enrollment rates increased from 65 percent to 95 percent, and their retention at 30 day follow up increased from 58 percent to 85 percent.

That is what we heard through our data collection through PCORI reports. This group actually published their learnings about engagement and the way it affected their project in JAMA Surgery, and we are grateful for that. Increasingly, we are seeing those publications from PCORI awardees. We also recognize there is a lot of rich learnings about the effects of engagement on our projects that come through PCORI's data collections, so we are now hearing from every project.

I want to take a moment to acknowledge this

particular partner, Aubrey Gibson, and the study team, including Drs. Dean and Minneci.

We will continue to inquire with our projects about the ways in which engagement is affecting their studies as they progress toward completion, and we have evidence already from both awardees and partners that some of the ways in particular that engagement is making a difference includes changes to their interventions or comparators, their recruitment strategies, and the outcomes they are going to measure, and how they are going to go about measuring them.

We want to direct your attention for a moment towards where this work is headed. We wanted to bring back this slide as a reminder that 2017 is the year where we can really turn our attention towards testing the associations between these characteristics of engagement that we have been working hard to document, like intensity models of engagement as well as specific phases at which engagement is happening, and the aspects of our studies that are of particular interest, like which

outcomes are being selected for study, the recruitment rates, and the time for study completion.

The reason we will be able to turn our attention to those questions now is because of our growing robust samples of data of projects that have matured to the point where we can answer some of these questions.

DR. FRANK: So, mindful of the time. Wanted to be sure to leave some time to hear from you, questions you have about these data. Our future questions involve using those intensity models as predictors and explanatory models of the impact, but we think we can look at variations by intensity level and also by the phases in which engagement takes place, and even by the effects that engagement is having to see if that differs by study type, for example, or by funding mechanism, programs, essentially.

We are really interested in understanding the effects of engagement on study operations, as you have heard, but also what impact is this having

on investigators, on the partners themselves, and on research institutions, since one of PCORI's goals is to influence the way research is done, and we heard a little bit this morning about potentially some changes to the way in which IRBs deal with research partners in terms of compensation. That is one example that we can then tie back to intensity models of engagement.

With that, I wanted to be sure to hear from all of you, your comments and questions about this particular set of questions.

DR. NORQUIST: Ellen?

DR. SIGAL: Thank you. I'm sure this work is really important. Until the very end, I didn't have any specificity of what it really all meant, and I think if we are going to spend this time and amount of money on research and qualitative data and analysis, we need to give specific tangible examples.

The idea of a trial changing because of hours is exactly what we need, or if they are asking the wrong questions. It is just too much to

consume, but if you can give simple, tangible real life examples of where this methodology has made an impact on a trial and for a patient, it would go a long way to helping us talk about the meaning of it, because it is all a whole bunch of interesting research, but not really tangible enough to understand what it really means.

DR. FRANK: If I could just respond real quickly, I appreciate that point, making it concrete. We did share with the evaluation strategy work group some specific examples, exactly along the lines you are saying, and we are happy to share those more broadly. In the interest of time, we scaled way back.

DR. NORQUIST: Francis?

DR. COLLINS: Thanks very much. My thought in listening to this is that perhaps the most interesting aspect of engagement, which you will confront momentarily, will be the impact of patients on data and results interpretation, and formulation of final manuscript and conclusions of the final manuscript, and you didn't mention that.

I was wondering why you hadn't included it, and you said in your introduction that you only included factors that you could actually collect data for. Any second now, I think that will be very important and may go to answer Ellen's question.

DR. FRANK: We do see some early examples of exactly that, patient and partners being included in the data analysis. That is something we look forward to growing more data on.

DR. NORQUIST: Ellen?

DR. SIGAL: People are spending a lot of money, spending a lot of time, and they want to know real world results. You need that elevated for each of those three, four, five examples, where this research has yielded major changes. Otherwise, it is impossible to comprehend. Everybody knows data and analysis and all this is important.

You need to give multiple examples of where this has changed the trajectory of a trial. Otherwise, it is going to be lost.

DR. SELBY: This is a great question and I know we don't have time to discuss it in depth, but

is that in your view more important than something quantitative? In other words, often times people want not examples but really showing in the book of projects, something has changed.

Recruitment rates kind of get at that. Other endpoints that will allow us to look at the whole book, rather than pulling out a few examples, or do you think it is just particularly with Congress, much more the examples?

DR. SIGAL: For patients and the lay audience -- of course, we have to hope this is quantitative and qualitative, that we have done our work. Nobody is impressed with all this unless you can say this is what changed as a result of it. We are spending a lot of money, and to justify your existence, and frankly to justify this research, unless it is research for research purposes, you have to have examples of how this has helped patients and how this really is meaningful work, and people have benefitted from this work.

I know when I work on my trial and I work with physicians, they will say to me, well, this is

a good scientific question. I said for who? There is a difference between the science methodology and the real world results that are coming to come from it, and this is what we have to be mindful of.

It has to be real. You have to think about frankly what patients are going to learn from this.

DR. SELBY: I think the trick, and you guys can all help us with this, is how you transform the anecdote into some kind of data that can be applied to every study. I think, Bob, you were starting to get into that a bit. Ultimately, did a study have impact. Perhaps some day even compared to studies funded by some other entity that doesn't push engagement so strongly.

DR. SIGAL: I think we have changed patient engagement in a meaningful way, but at the end of the day, you have to have an example to show. I'll give you an example. 60 Minutes is doing a big program on the moon track. Everyone is excited. The moon track was just announced a few weeks ago.

That is what people are looking for, okay, so you have it, it's a big deal, give me tangible --

show me a patient who has benefitted.

DR. NORQUIST: Bob?

DR. JESSE: This is one of the challenges in health care because health care is driven, decisions are driven by anecdotes, not necessarily by data, and the plural of anecdote is not data, but telling the story is really important, as you say. Telling one person's story that was helped can communicate a lot more than tables and spreadsheets and graphs.

DR. FRANK: Yes, point taken, absolutely. We are pleased that we are able to communicate with credibility to the research community as well, based out of the qualitative data.

DR. NORQUIST: Leah?

MS. HOLE-MARSHALL: I'm trying to reconcile a little bit of the data here with the last presentation that we heard from the payer providers. One of the lowest groups with engagement is the one that is the most invested, using that word sort of generally, in both the success for themselves, in this group.

Is there an effort to increase the payer engagement in 2017 before you get to the 2019, these are the outcomes, in your logic model? I hear the discussion about lower back pain and some of the other pieces that have come from discussions we had earlier today around high cost drugs and things like that.

My immediate sort of sitting here, if we don't engage that group in this research, the next two years are going to be harder than the last.

MS. TROEGER: I wonder if I could just grab that question? Yes, over the last two years, we have had a really enhanced effort to engage the payer and purchaser community as well as the clinician communities. Prior to today, we have been bringing in clinicians, payers and purchasers, to meet with the Board. We have also met with them individually, had several roundtables.

One of the challenges is getting the payer and purchasers engaged on individual levels, and I think part of that is because of the challenges they have getting away from what they do during the day.

Engaging them is a little bit different than engaging patients, but absolutely, it is a huge commitment that we have made.

DR. FRANK: I think the fact that there is engagement in the research projects and then there is attention to different stakeholder groups and end users of the information that is coming out of the work that PCORI funds, so by having these data, we are able to have those discussions and to know.

MR. BECKER: One of the things James said on his way out was he previously worked for the March of Dimes, and we got input from the March of Dimes, and before coming here, he actually cross referenced what he sent in versus what we are doing, and he said there was a significant amount of stuff that we are doing that was on that list. We need to encourage them to keep giving us that.

DR. SELBY: I just wanted to respond to Kathleen, one of the reasons you see the increase from 7 to 15 percent is because in the last two years, we have started funding big projects. We say big projects must have payer engagement. We didn't

have any big projects two years ago to speak of. I think that is a big driver. They can't be involved in every little study, that we require them to be involved in the big studies.

DR. NORQUIST: Thank you, Lori and Laura, very much. I'm sure we will have other reports as we go on.

Evelyn Whitlock, our Chief Science Officer, will be giving us a report on research synthesis.

DR. SELBY: As Evelyn is sitting down, I just want to say to be very clear that we see evidence synthesis and dissemination, the kind of activities that the employers were talking about and others, as just like that, you have to make sure you have the evidence right.

Evelyn will be talking today about the evidence synthesis initiatives we are starting, and you have heard and you will continue to hear about dissemination efforts.

DR. WHITLOCK: I do have slides, and there they are. I have just a few slides today, and I know I am between you and a break. I'll try to keep

it upbeat and interesting.

What I'm going to be talking to you about today is an overview of a program we are starting in research synthesis, which is a broad umbrella term, and I am going to focus in on evidence synthesis, which is a subset of what we are doing in systematic reviews.

At a high level, I want you to understand that we are looking to focus on producing products that are actionable, that are relevant, that are rigorous, that don't duplicate. There are lots of systematic reviews going on around the world in other syntheses, so we are looking to compliment what is being done and add value.

I'll go into a bit more detail about that, but I thought you would want to understand as we go to design this program for PCORI.

As you are all well aware, and it was good to be reminded that you went through and looked at the legislation with highlighters, you are aware that the authorizing legislation states evidence synthesis is a core function of PCORI, and that one

of the ways that PCORI will assist its many stakeholders in making informed health decisions is by advancing the quality and relevance of evidence through research and evidence synthesis that considers variations in patient subpopulations.

It is clear from the get-go that the writers intended both research and evidence synthesis to be part of the products that PCORI uses in fulfilling its mission.

It's interesting because this is a very common term, "evidence synthesis," but it is really hard to find a definition for it. Kind of like art, people think they know it when they see it.

I think the best definition is that it is a set of methodologies, so it is not just one thing, but it is various methodologies that are used to integrate evidence from variable sources in order to get to a better answer, something that is more comprehensive, something that focuses just on best evidence.

We all know that one study is one study, and there are some landmark studies that get

produced, but knowledge really generally develops through the accumulative effort of a lot of small kinds of efforts. Even if you have a big study, you still would like to know -- because that big study can't represent all that might benefit from its findings -- you would like to know if that big study is consistent with other research that has been done that is also relevant.

It takes us beyond the individual study. It allows us to begin to be more confident about what we know in terms of agreement and disagreement, and allows us to look at those things both quantitatively and qualitatively.

Importantly, and you already called for this in the methodology standards, if you are going to not duplicate what has already been done in a way that is unnecessary, then we know where there are true gaps in the evidence.

If we are going to be replicating studies because we need further assurance, that's one thing, but if we continue to do the same research because we didn't look carefully to be sure that research

wasn't already done, then we are wasting the dollars that are given to us and we are not producing value.

If you go back to the evidence synthesis concept, I have laid out here a couple of the different kinds of methodologies that people use, systematic reviews, rapid reviews, decision models, and then even within systematic reviews, I'm going to call out for you different analytic approaches.

The kind of meta-analysis that most people are familiar with is really in a more precise term called "aggregate data meta-analysis" or "study level meta-analysis." It is relatively simple to do in that you use the published evidence or you might go and ask for unpublished evidence if you're aware there is work that hasn't been published.

You are basically taking the information that has been summarized at the study level, so it is the average treatment effect usually, and you pull that together where it is appropriate.

Now, there are other ways of pulling those data together. What I'm going to be talking about in some depth today is the idea of individual

participant data, level data. There is network meta-analysis and others.

As we begin to go into these various analytic techniques, what we are looking to do is align analytic techniques with the mission of PCORI, particularly to produce evidence that will say what treatment works best for whom and in what circumstance.

Let me step back to the research synthesis overview and talk about it as an umbrella term. Think about it as an aggregate of activities that we are doing using tools and methods that synthesize information to create knowledge.

We are covering a range of activities with this, even though our legislation calls for evidence synthesis alone, we are also looking at this issue of reusing research data. One of the things that the research community talks about is the fact that we don't get all we could get out of trial data.

You are aware the New England Journal of Medicine is sponsoring an opportunity for people to reanalyze the STRIVE data because there are

additional things that can be learned.

We are very interested in this aspect of evidence synthesis so we can get at exploring variation in treatment, and start to produce evidence that is more personalized.

Similarly, we are looking at even as we wait for some of the results to come out from our research investments on individual studies -- we believe there is a value in helping to communicate our portfolio.

Beyond the portfolio cluster analyses, which were started before I came, we are starting some mapping of our portfolio, which would communicate some of the lessons learned, as well as help people interrogate our portfolio in real time, even before the results are available.

We are starting this in an area for care transitions, so that people will be able to see what are we studying, as well as we are looking at it for community health workers and telemedicine. We believe that will feature some of the key areas that PCORI is making fairly large investments in, in a

way that will make more visible -- I think one of the speakers from the employer panel said we can't really figure out what you are doing, help us know what you are doing. I think this will be one way. It will make it quite clear and interactive.

Finally, we are looking at other tools. I'm not going to spend a lot of time on the bottom two, either the portfolio synthesis or evidence maps, but I'm happy to come back in the future and talk more about those, particularly as we have some specific examples from our own portfolio.

DR. LEWIS-HALL: Can you walk me through the timing, just for clarification. In the specific topic area, you would say okay, what do we currently have for review, then how we would redeploy data in that space, then what is PCORI doing to plug the current holes, and then what are the existing holes that remain. Is that the picture we should expect to get at the end of that?

DR. WHITLOCK: No, it's not. All of these are not integrated into one slope. I'll go on and I think it will be clearer. Each of these activities,

it's not that they are completely separate, but each of these activities has its own flow.

In essence, the evidence synthesis and the research data reuse are opportunities that could happen just through our topic pathway. I'll show you an example with something that came from the March of Dimes. It's not quite as method as you are suggesting, but I will show you how it fits together.

In laying this out in a broader perspective, I wanted to focus on three things to begin with, given that it is late 2016. What I wanted to do was first really think about what could we do in the short run that would address heterogeneity of treatment, more personalized individual health care choices. Those are the kinds of things that if we can find robust findings, get them out, they really can make a difference for people right now.

We are looking at more rapid deployment of actionable CER evidence. I will show you the details of that. We are looking to update existing

comparative effectiveness research reviews that already contain actionable information that are a year or two out of date but could be brought up and then given to our dissemination and implementation arm to produce tools for all of the various stakeholders that are interested.

The issue of communication of our current portfolio to make it more visible as people had asked for.

I want to say that what we are focusing on right now is really relatively rapid turnaround. We are thinking about what can we get done in a year or two. Even though evidence synthesis is more rapid because most of the evidence is gathered, it doesn't mean it's quick under the kind of time frames that we are operating.

We really are focusing even within this set of activities on what can we do rapidly that is also robust. It needs to stand up to very high standards but it needs to get out quickly.

That is what it says here. Short-term turnaround, rigorous, relevant, CER or heterogeneity

of treatment effect. I am going to do this in two ways, beginning with generating some new research products, individual participant data meta-analysis, and other relatively rapid opportunities to reuse existing research data.

Then also as I mentioned, setting up a surveillance system to locate and qualify existing systematic review products that address comparative effectiveness research that have actionable evidence for one or more audiences, and then working to update and disseminate these alongside AHRQ.

There is just a quick overview. You have the portfolio, you have the research data reuse on one side, and in the middle, we have surveillance of existing CER systematic reviews, and then the portfolio analysis, mapping, and communication that I'm not going to talk about any more today.

Under research data reuse, there are three major categories of work that one could do. One can take the evidence from systematic reviews, go and contact the trialists, gather all of the individual participant level data, and perform robust meta-

analyses to get at individual characteristics and drivers of both treatment benefit as well as well as potential harm.

One can also in a systematic review where there are a lot of indirect comparisons where we have comparative effectiveness research. We have studied A versus placebo, B versus placebo, C versus placebo, and a little bit of B versus C.

You saw earlier the networks that Joe put up. That is another way that we can generate through statistical techniques some series of comparative effectiveness that builds on trying to adjust for differences with indirect comparisons.

That can get us some evidence in the lack of definitive evidence in a shorter term, and then pivotal trial predictive analyses. Interestingly enough, PCORI has already funded both the network meta-analysis you saw earlier, as well as pivotal trial predictive analyses.

These are clearly in our wheelhouse, but I am looking for us to identify a stream of opportunities here because they can produce

actionable -- individualized evidence and comparative effectiveness research without a five year time frame.

I am going into this area talking about these reuse opportunities, which I already did. They are not applicable to everything. When would you want to reanalyze data? When is it worthwhile going back and getting all the trial data for individual participant data meta-analysis?

It's good when you know or expect there is a range of treatment effects. Interestingly enough in pragmatic clinical studies, because the inclusion criteria are much broader, these techniques become very much more important because we do need to understand across the diversity of participants who benefits the most.

It also is very important when we know that you have to go beyond average. We can, as I said, generate relatively rapid actionable results. I think one of the other important parts of this is it gives us an opportunity to generate a relatively unique funding niche for PCORI.

It's not going to be a huge area, but it complements the other things we are doing, and right now, we are identifying it as an area of funding that really nobody else is taking on. I think as we move forward in open science that these sorts of opportunities will become more and more important because as data become available, our opportunities to reuse data appropriately and responsibly and to the public good will become even more available.

Having funding mechanisms and method standards and analytic techniques in place really puts us in a good position for the future.

I'm going to talk a little bit about individual participant data meta-analysis, and I've said that you get the individual level data from all the trials. It is considered to be the "gold standard" of meta-analysis for many, many reasons.

You can standardize variables in analyses across studies. One of our limitations when we do study level meta-analysis is we are stuck with what they have reported, and the way they categorized the data, and the way they defined the outcome.

If they didn't gather the data, you obviously can't fix that, but you can standardize quite a bit. You can also correct data, so there might be there are data errors.

I think the real reason we are interested in it is not just better quality but because of the second area, this is the only way that you can really get to subgroup effects, particularly based on multiple factors.

We don't go through life, and I'm a female, and I'm not going to tell you how old I am, but I am a female and I'm in that age group, too, and we also look at subgroups by sex, by age, but not together. As we know, people with multiple comorbidities are an amalgamation.

It is a way that you can look at data when you are interested in these multiple factors together, through individual participant data meta-analysis and predictive analytics and that kind of thing.

These are really important techniques for us to be able to bring to bear. It gives you a

clearer way when you go do a systematic review. We do critical appraisal. You want to make sure that the studies were designed and conducted in ways that don't introduce bias. You can actually do a more accurate risk of bias assessment when you have the individual participant data and information from the protocol.

Sometimes there is additional follow up you can do. Also, you can do different analyses. We often have a single time point but with full data, you may be able to do time to event analyses which were not part of the original opportunity.

I am going to talk about the surveillance activities that we are undertaking. There are systematic reviewers around the world. ARHQ is one of the biggest producers in the United States and funds the most systematic reviews with a big focus on comparative effectiveness research. They produce a very important body of work. Others around the world also produce some work this way.

It's very important, and one of the big challenges in the worldwide producers are not just

quality but being able to keep these up to date. These are a lot of work particularly when they are volunteered. It is when they say oh, my gosh, I had no idea how much work this was, and then it is hard to get it updated.

Similarly, in AHRQ, who has a real commitment to keeping these updated, it has some limits in its funding. It may have to prioritize.

There is a real importance if you are going to bring evidence to decision making, that you are bringing current evidence to the floor.

What we are doing here is really filling a niche, servicing the need for up to date information in the public domain around important comparative effectiveness research issues.

I have a more detailed screening approach, we will be looking at important topics that are relevant to U.S. health care decision makers. The reviews need to be of a sufficient quality because there is a lot of not very good systematic reviews out there.

They need to be really relevant, and

particularly they need to have either already produced actionable evidence, it just needs to be updated, or there needs to be the possibility that an update will produce actionable evidence because there is a lot of intervening knowledge from the time the first review is done and now, so we have a good opportunity to get there.

We have been told time and again that decision makers can't use a systematic review that says there is no evidence. We don't want to spend any time on those activities at this point.

If some of these meet all the other criteria, they are things that our dissemination and implementation arm, which is working very closely with AHRQ, can work on turning into translation products. If they are out of date, they can be updated. We are working with AHRQ right now to try to set up a memorandum of understanding so they can update some of their reviews.

I'll close saying this is a quick update on what we are doing as part of the IPD meta-analysis. We are working on a pilot project. This actually

came from engagement with the March of Dimes. I have now traveled. Poor me. I had to go to Sweden and London. It was terrible.

We met with trialists around the topic of progesterone and pre-term birth. The March of Dimes is involved with this and the National Institute for Health Research is also involved.

We are looking at the three of us funding individual participant data meta-analysis that folks like the World Health Organization and others are thinking will be very important in guideline development. It certainly will help to figure out who benefits from this treatment in this very important condition.

As part of this we are doing some really exciting work establishing governance standards and funding streams for this type of work. We have worked carefully with the trialist community, and have set up a structure that we are very excited about.

As Robin said, we have asked the Methodology Committee to help us look at producing a

new methodology standard so all of this work can move forward with an established methodology standard. We are starting to do surveillance, as I mentioned. As we get into understanding the opportunities that we have, we will look at integrating them within our topic pathway.

Sometimes the next right answer, and I think the IPD meta-analysis example is prime, sometimes the next right answer is not another trial, it is not an observational study, it might be a systematic review or it might be something like an IPD meta-analysis. I feel like we are at the right point with the right answer for this particular one, which makes it very exciting.

Finally, we are looking for other potential opportunities and how to establish a pipeline for some of these more novel kinds of activities.

I will stop there and see if there are any comments, questions, concerns, and look forward to hearing from you. Larry?

MR. BECKER: Two things. I wish our panelists who were just here had stayed and listened

to this. The second question, I'm not sure I understand how this works, so I'm going to ask this question.

Are you planning to publish a book of actionable findings, Volume 1?

[Laughter.]

DR. WHITLOCK: Good idea. I wish. What we are planning to do is we are planning to get those to Jean and Joanne in the dissemination and implementation area so they can take all of this valuable information we got from stakeholders about how they want to see these things and get it out there. We hope the book is disseminated at the point of care and point of decision-making.

DR. NORQUIST: Barbara?

DR. McNEIL: That was very interesting. The last point, I think, is a critical one, identifying projects that can go forward that will have the individual patient data available. Do you have any sense of a list of those and what investigators will give you the individual patient data?

I ask this specifically because I know Blue Cross has tried on a number of occasions to get these data, and it's really very, very difficult.

DR. WHITLOCK: I understand. I think one of the interesting and fortuitous situations for the first one we are working on is the willingness of the trialists internationally to bring this data together. I believe it is 39 or 40 randomized control trials.

DR. McNEIL: I was thinking of the new ones.

DR. WHITLOCK: The new ones, I would like to talk to you about that a little bit in the future. I do have some ideas about how we can set up a structure, but I need to work it through the SOC first.

I have outlined on the white board in my office how we can set up a pipeline for these, because I do believe there is a way to do that, and I believe it is an important thing for us to do, and we should push forward with it.

DR. McNEIL: I think one of the things that

we found, very few investigators are willing to give out individual patient level data, and when they are, it takes an incredibly long time negotiating information with all of the participants that collected the data, and then getting all kinds of data use agreements and whatever.

While I think this is extremely important and it would be wonderful to do, the speed with which you would have to go forward on this to have actionable results to meet some of the concerns of our prior panel would be like lightning.

DR. WHITLOCK: Let me give you the time line for the progesterone and pre-term birth.

DR. McNEIL: I was thinking of the next one.

DR. WHITLOCK: I think the other thing we are working on out there in terms of the governance standards, we went to London, we went to Sweden, and they were very nice, but they didn't really know who we were. They knew us a little better, and then we went to London. We got drilled pretty well by the trialists about what we were proposing.

We proposed a structure, a set of governance standards and structure, that would allow minimalization of conflict of interest, but participation with the trialists in a way that the trialists agreed would be worthwhile.

I think the other benefit we have in this particular group is you have a lot of people who are very committed to this topic and are willing to plow the field. The feeling at the meeting, and again, these were trialists, folks from NIHR, folks from the March of Dimes, was we were setting out a template that might be reproducible in other kinds of situations.

I believe the tide is with us. We are moving into open science. I believe getting a test case is a really good thing to do, getting a governance structure that seems fair and equitable, and then hopefully it will all align. I take your point, it can be challenging.

DR. NORQUIST: Andrew?

DR. BINDMAN: Thanks so much, Evelyn, very nice overview. I just wanted to maybe share a

little bit with other members of the Board that I really have appreciated both your calling out and of course, your direct knowledge of the historical work that AHRQ has done in this area, and thank you and PCORI staff for finding ways to work in alignment with AHRQ around the work on comparative effectiveness and systematic reviews.

I think this is very important both in terms of expanding the capacity of what can be reviewed, but also to make sure that there isn't confusion. We don't want to add multiple places of confusion where users of this information are uncertain about where to go and find it. I think bringing alignment is really helpful in the ways you are pursuing it.

I think we will have to continue to try to -- it is important, I think, to continue to try to work on this alignment together because as many know, AHRQ has had questions raised about redundancies in different areas, working with PCORI or others, so we want to make sure we do stay in alignment.

I think the way you have identified working together looks very positive in that regard, but I think this is an area of continuing discussion that needs to happen because if there are issues where PCORI and AHRQ are not aligned around doing these kinds of reviews, then I think AHRQ would also have to evaluate its capacity to continue to work in that area.

It would just have a net impact on the capacity of being able to do this from AHRQ's perspective, and I just want you and others who have talked about this to appreciate that. I think it works very well in the way you have discussed, but it is something we are going to continue to evaluate along with you and appreciate the work you have done so far to try to bring that into alignment.

DR. WHITLOCK: Joe, did you want to make any comments?

DR. SELBY: Just I think, Evelyn, to acknowledge that we agree with Andy's analysis that we need to be able to explain clearly and with one voice how we work together to avoid duplication, how

we complement each other, avoid redundancy, and both work for the same goal of getting evidence gaps filled.

I think we have all worked in good faith, and there are some challenges that we will have to keep an eye on as we go forward.

DR. NORQUIST: Bob?

DR. JESSE: Getting to the spirit of open data but really being able to do that drilling down to the patient, how much are the issues around identification?

DR. WHITLOCK: In the previous individual participant data meta-analyses that have been done, obviously the identified data had to be provided. I think that has been part of the data use agreements. Are you asking how much those procedures have created some of the delays? Maybe I'm not understanding.

DR. JESSE: I should have maybe put it in context. We are having a lot of issues with our ethics people about sharing even de-identified data that wasn't specifically part of a front-end

consent, because of the question about can one really and truly de-identify data.

DR. WHITLOCK: I think that is a very interesting question. I think it is a little bit of two separate issues. Do you need to separately consent. I think Barbara alluded to that, which is going to be an issue across any kind of open science aspect.

Second, in terms of identification, the way that we are working now is the data will be held by a methodology group, and it won't be put in the public domain.

I'll be clear, that the National Institutes for Health Research is interested, once you bring data together, to do an individual participant data meta-analysis, and once you harmonize those data and standardize them, they would like to have them voluntarily put into a repository so you would have living data and as more trials come out, you would actually be able to update the analyses.

NHR will potentially fund that data repository opportunity but it won't be a requirement

for people to be willing to provide their data in this limited set and in a constrained and controlled environment.

DR. NORQUIST: Alicia, if you could make it quick.

DR. FERNANDEZ: Very quick question. I'm curious, following up on what the panelists before said, whether we had any discussions with the people on up to date or other informatics, things that are already woven into informatics so as to be able to rapidly go from evidence synthesis into something that people can read, particularly at the same time or right after the peer review.

DR. WHITLOCK: That would be a good thing to talk about with the dissemination center. Maybe they have been talking about it, I'm not really sure. Jean can answer.

MS. SLUTSKY: We have been talking with many different massagers of data, sort of secondary packaging of data. That is ongoing right now. We actually have a translation center that encompasses a lot of experts in this field, through a variety of

agreements and subcontracts.

DR. NORQUIST: Thanks, Evelyn. We are going to take a 10-minute break. We have two things we have to approve, and public comments.

[Recess.]

DR. NORQUIST: Why don't you start?

DR. SELBY: We're broadcasting again, and I'm going to assume some Board members are still standing but they are listening attentively.

This is a discussion that has been going on for a long time. You will remember other versions of it at Board meetings before. For the last six to nine months, we have been talking about it really quite regularly at the RTC, and with the RTC and also with -- actually, both Steve Goodman and Harlan Krumholz are on the RTC officially.

Within the RTC, we have advanced the draft policy, PCORI's draft policy on data sharing to the point that we believe, and members of the RTC, I think, believe with us, I know Harlan and Steve particularly are anxious to get this out for public comment, so I want to introduce Jason Gerson, who

you know.

I want to introduce him in order in part to thank him for his hard work on this, and I also want to mention Nadine Peters from our Legal office, who has also played a lead role in getting this to this point.

I will just say this, and Jason will say this, too, this is a sticky area. We really are not that anxious to go way, way out to the end of the limb, so this is a policy that has at least some questions still unanswered, but we are anxious to get it out and get a sense of the community, and bring it back to you after we have incorporated those comments.

Thank you, Jason.

DR. GERSON: Thank you, Joe. Before we go much further, I just want to also acknowledge the rest of the open science work group that is comprised of six other PCORI staff members across science and some other departments that have been instrumental in advancing this work, too.

Freda, did you want to make any remarks?

Freda has had an instrumental role leading the RTC through this.

DR. LEWIS-HALL: Just really quickly, I want to contextualize this. You all heard a little bit this morning, we discussed and answered questions, and heard a little bit about what is happening in open science from PCORI's standpoint. These are things that are pretty much underway at this time.

What we are really talking about now is putting out for comments what I'm going to call a potential next step or potential next opportunity to move that step one step beyond where we are today.

How do we make the datasets, the study protocol, and other elements' potential to be used in an open science environment. I think what we talked about this morning is kind of -- Joe is calling it a "limb," I like to think it is a runway, that we are out on the runway now with some important open science opportunities. This is getting thinking and input on the potential next steps.

Let me say again thank you, because this has been a lot of work I know for the staff and getting the input and collecting. Thanks to all that have given input inside PCORI staff, on the Board, both the RTC and SOC, and other members who have a passion around this, as well as others that have given us input and insight to help move this along.

DR. NORQUIST: Thank you, Freda.

DR. GERSON: I'll just walk quickly through a brief number of slides. The main objective of the draft policy is really to set forth PCORI's expectations and guidelines for our research awardees, for the management of their data, for two main purposes.

One is to facilitate reproduction of original analyses, and the other is to promote data sharing to enable conduct of additional analyses using data from PCORI funded studies. We imagine the latter is where most of the action will be. I don't know how much desire or intent there will be to fully reproduce PCORI funded studies, we shall

see.

The draft policy was developed by PCORI staff. We have had input from an expert advisory group, as well as from the RTC, over the last several months. We have also engaged in discussions with some other funders and regulators of clinical research, and we have received in the last month some detailed comments on the draft policy from NIH, the version that was shared with all of you.

Just hitting some of the key highlights of the draft policy, the main intent is for PCORI funding to support the deposition of data as well as data documentation. This would include the study protocol, the metadata, and the analytic code.

For studies funded through the pragmatic clinical studies mechanism and the targeted funding announcement mechanisms, it will include a requirement for all studies to prepare data for data sharing with funding provided by PCORI for deposition in the data repository on a case-by-case basis.

We are starting by focusing on some of our

larger investments with the idea that as the results roll in, they are of interest to the scientific and research community, we will be prepared to fund data sharing for those other studies as well.

In this draft policy, we have articulated a requirement to maintain the data in a repository for a minimum of seven years, and we will support that through at least a seven-year period, depending on where we land with the final draft policy.

You will see, the policy by design is somewhat thin on the operational details. That is by design. We feel we still have a lot to learn. We want to learn from the public through the public comment period, and as I mentioned before, we are engaging a pilot project in which we will bring together a number of our awardees, six or seven of our awardees, including some pragmatic studies, with some data repository organizations that run repositories and data sharing platforms.

The goal of that pilot is really to do some learning about the key challenges and opportunities with getting their data and data documentation into

the repository and ready for data sharing with third party researchers. That is the pilot project.

We are in the process of evaluating the proposals from the repositories. We imagine by the time we get done with negotiating with the finalists for that role, launch the pilot, late 2016 or early 2017, and the pilot will last -- we don't envision it will last more than three months.

That is what we planned for, a three month kind of engagement between our awardees and the repositories should allow us to do the learning we need to do that will inform the next version of this policy.

Pending your approval today, we will plan for a 45-day comment period for the draft policy. We feel it is adequate time for the public to weigh in, and we will advertise and notify the public in various ways that the policy has been posted for comment.

We have also developed an open science work group joint with some input from the RTC on developing targeted questions that will focus the

public's attention on a number of important issues related to the policy. Those questions were shared with you.

They include a question about the appropriateness or the length of the retention period, the qualifications and credentials of the people who are requesting data, and kind of what represents reasonable data repository standards, at a minimum, what kind of attributes should those repositories or platforms have to be acceptable to PCORI organizationally.

Of course, we will ask the public for their comments on different consent models that are related to the policy.

We sent those questions to you in the hopes that they may have prompted some more thinking or additional questions. We will have to incorporate those into the public postings.

I'll stop here and take any questions or comments.

DR. NORQUIST: Rick?

DR. KUNTZ: I think this is a really

important initiative for PCORI. I was wondering, there are several entities trying to do the same thing, understanding how to operationalize the data, one of which is the National Academy of Medicine. In fact, they have a meeting this week on operationalizing open science.

The other is the National Evaluation System for Health Technology that the FDA has initiated called NEST. That is going to be a process to understand how to operationalize data sharing perspectives, working with J&J to actually do the operational component of that, they have a very slick system of managing the data and putting it into a form that can be shared.

Of course, Harlan's program, YODA, has done more of this probably than anybody with respect to actually sharing the data publicly.

How do we get that kind of experience together because there are a lot of lessons we can learn from those entities.

DR. GERSON: We are mindful of many of the things that you mentioned. I think for us as a

funder, we want to try to get our head around both some of the operational challenges of what it means to get your data managed properly so it can be deposited in a timely way.

I think the pilot is only going to involve a very small number of repositories, but the goal there is to do some key learnings, not just about the features and governance models of those repositories, but to figure out what attributes are most important for us, and then on the back end of the pilot, we will be kind of engaged in doing another procurement for the broader data sharing community.

Our goal here is to land on probably a selected number of repositories that we recommend to our awardees, anecdotally what we have heard is our awardees would like us to be a little prescriptive and to direct them to certain repositories, so we will have to do some more learning first. We are not doing this in a vacuum. We are mindful of the NIH model, Harlan's work, obviously. We won't go too far afield without being involved with those.

DR. NORQUIST: Larry?

MR. BECKER: So, maybe I missed this. Three questions. Who owns the data? Assuming that we own the data, what's the retention strategy for this and who decides under what circumstances and for how long?

MS. HENNESSEY: Excuse me. One question on the data, PCORI does not own the data for the research that it funds. From the very beginning of PCORI, the research institutes own the data. We actually have taken very careful steps at least in the pilot, we don't want as an organization to house the data ourselves, that requires highly sophisticated systems and platforms to do that.

I just want to make sure it is understood that based on PCORI's long-standing model from its inception, the data is not owned by PCORI. As a funder, we can and are intending to include requirements about what should be done with the data to make it available, but this is what the pilot is about and getting the draft policy out for comments.

DR. GERSON: Thank you, Mary. As far as

the governance, what the adjudication process would look like, that's something we will also learn from the pilot, and probably we will kind of work with the repositories we end up selecting about how those requests are adjudicated, whether they constitute requests from clinical qualified investigators, and whether the inquiry itself represents a reasonable scientific request.

Organizationally, as Mary said, we are trying to position ourselves to encourage our awardees to make the data available but also not put too firm a footprint on how those requests are ultimately adjudicated.

DR. NORQUIST: Mary, do you have a follow up?

MS. HENNESSEY: No.

DR. NORQUIST: Mary, I assume as part of the contract, we have the right to ask the contractee for certain things; right?

MS. HENNESSEY: Yes, we can use our funding contract, for example, for several years we have required our recipients to have a data management

and sharing plan. That followed on a long-standing requirement in our PSA, that our applicants be developing a data management and sharing plan.

The tools that a funder has at its disposal like PCORI to move forward and encourage its recipients to advance its ability to share data don't have to depend on the funder owning the data, so that are the steps, I think, that are being taken right now.

DR. NORQUIST: Do you have another slide? I thought there was a motion.

DR. GERSON: There is a motion. I am sorry.

DR. NORQUIST: We need a motion. Basically, what we are doing is just approving the posting for public comment. Do I have a motion?

DR. GOERTZ: So move.

DR. NORQUIST: Second?

DR. JESSE: Second.

DR. NORQUIST: Any other comments or discussion about this motion?

DR. ZWOLAK: Just to point out there has

been lots of active discussion about this in the journals, including the New England Journal last week, an article labeled “Is the Juice Worth the Squeeze.” I think the information that we derive from public comments may well be telling.

DR. NORQUIST: We have to do a roll call vote. I don’t know why, since we can see everybody.

DR. COLLINS: You can’t see me, but I vote yes.

MS. HENNESSEY: Gray, you’re not committing money, so I think it is fine to do a voice vote or hand vote.

DR. NORQUIST: Hand. Everybody in favor, just raise your hand.

[Show of hands.]

DR. COLLINS: I’m raising my hand.

[Laughter.]

DR. NORQUIST: Okay. Thank you, Francis. I don’t think Allen is on the phone. He dropped off. I didn’t see anybody that didn’t raise their hand, but just in case if I missed someone, is anybody opposed?

[No response.]

DR. NORQUIST: Does anybody abstain?

[No response.]

DR. NORQUIST: Okay. It's unanimous. Thank you.

The next one is Evelyn. Topic for Sequential Targeted PFAs, Back Pain. Since we all probably have back pain after sitting here all day long, Christine, we may need some manipulation or something.

DR. GOERTZ: I'll be glad to tell you what the research shows on that.

DR. NORQUIST: Evelyn?

DR. WHITLOCK: Bob, do you want to make any introductory remarks?

DR. NORQUIST: I'm sorry. Bob Zwolak, who is the chair. This came down to the SOC; right?

DR. WHITLOCK: It did.

DR. ZWOLAK: Thank you. My comments will obviously be brief. We're going to talk today about the concept of sequential targeted PFA, which is an outgrowth of our learning and distinct from the

motion we passed a couple of meetings ago for reannouncements of established PFAs.

The former reannouncements will be the exact same as the initial announcement, potentially with very subtle changes if we have answered a question or two on the original. Sequential is a product of our learning experience, and is relatively a new concept.

With that very brief introduction, Evelyn, you're on.

DR. WHITLOCK: I want to thank the SOC, many of the members and actually others on the Board, who helped us work through this particular targeted funding announcement. I'm very grateful for that kind of help, thank you.

Just to remind you, I know this is very small, but we go through a process that includes a lot of stakeholder input, a lot of refinement, development, at various points at which something can come out of the pathway.

When we get to the bottom of this -- this process, I believe, I've been told, it takes about a

year, when we get to the bottom of this process, we end up with targeted funding announcements or pragmatic clinical studies.

We are looking at getting more bang for our buck out of the investment that we make in this process, and the target is putting out additional targeted funding announcements in areas like low back pain is an example of that.

I think you have seen this previously because we have issued several funding announcements in opioids, and they came out of the same pathway. This is building on a concept that you have seen before that we think makes sense to generalize.

Let’s go back and look at the history of this topic within PCORI. This was identified by you as a high priority topic in December of 2012, and it has come up through a number of our engagement activities with the Americas Health Insurance Plans, with the National Business Group on Health, and certainly with the American Physical Therapy Association.

I think you heard in the employer panel

that chronic low back pain would be a priority. I wish they would have stayed for the afternoon because maybe they would have liked to hear this.

We have had a number of stakeholder workshops. The first was in March of 2013, in which we had a webinar looking at treatment options for back pain. We had a prioritization meeting in June of 2015 looking at comparative effectiveness research questions for treatment options focusing in on chronic low back pain. In January of 2016, we reconvened the group to get further input.

We actually have had a low back pain topic listed as part of our priority pragmatic clinical studies listing. This has actually made it into both a targeted funding announcement and a priority clinical studies area. There are slightly different focuses.

The one that is in the pragmatic clinical studies priority topic is a topic that focuses on preventing transition, so folks that have acute low back pain, you'd like to not have them go into chronic low back pain because that's where much of

the morbidity and long-term treatment is, et cetera. Being able to deal with preventing that transition is obviously very important for patient-centered outcomes for insurers, et cetera.

That particular announcement has been up in a number of sessions, and we funded a couple of studies in that area.

In terms of targeted funding announcements, we did put out a targeted funding announcement that you approved in March 2016. It was opened in April. We received five LOIs. We invited four and two applications were received. We hope to announce awards in January 2017.

This is a very focused targeted funding announcement. This is looking only at the comparison of lumbar fusion surgery versus optimized non-surgical multidisciplinary programs in patients who are candidates for surgery and have non-specific, non-radicular chronic low back pain.

It's a very specific targeted question. It is one that is completely adherent with some of our stakeholder interests.

What you are going to see today is there are a lot of other questions that other stakeholders have, and that are important evidence gaps in our knowledge about how best to manage chronic low back pain, and that is why we would like to issue another targeted funding announcement.

This is more of the rationale. This is a high burden disorder in the U.S. It affects somewhere between 5 and 10 percent of adults, and it accounts for a lot of the costs borne by low back pain. I think it would account for all of it. The chronic is accounting for a lot of the costs. Sorry about that. The costs associated with this is really around the management of those with chronic rather than acute low back pain.

I mentioned our previous targeted funding announcement, and I mentioned that we had this as a priority clinical study, but we have gotten two studies thus far that look at that transition, certainly haven't even covered the waterfront in that area, but we do have two studies in that area.

We continue to hear from stakeholders, and

we saw a recent 2016 systematic review that confirmed our belief that there are many important evidence gaps that remain that could be important to close to improve care in this area.

This is a synopsis of the systematic review done by Chou, et al, looking at the research needs that remain. The point this review made is that although we have recommendations and guidelines for low back pain, only a small number of those have moderate strength of evidence to support their use

This is one of the most vexing areas for clinicians and plans and payers, it is uncertain what combinations of therapies are the most effective or sequences. We get asked this question a lot. What should we do in sequence, what are the best ways to put these things together. This was called out looking at both pharmacologic and non-pharmacologic interventions as a need and certainly an evidence gap.

It was also called out in this review that there are specific subgroups that we are uncertain about whether the benefits differ.

This came out when we were talking to the primary care clinicians about the importance of this topic, and they said yes, we have specific issues around people that are also obese and how you manage low back pain most effectively with them. We have issues with older adults because of multiple medications. We have issues with people who are working age and who have manual jobs, these are complicated. There are some subgroups that are important to think about.

As with many conditions, there is not a lot of information on longer term follow-up or the kinds of outcomes that the employers called out today, besides pain and function, ability to return to work, return to premorbid function quality of life.

There are a number of guidelines, some of them are being updated. The guidelines to date have generally focused most on the management of acute rather than chronic low back pain. Mostly when they do talk about chronic low back pain, it is sort of like a menu of options, many of which don't have very strong evidence, at least in the synthesized

format, and without much evidence on how to sequence or combine.

This is just an illustrative. This is not the state of the science, so I don't want you to think it is. It just illustrates to you the disconnect between what was recently summarized in the Chou systematic review and what's recommended.

On the left are the interventions that within the Chou systematic review have at least moderate strength of evidence, pharmacologic and non-pharmacologic, and on the right are the treatments for low back pain, and the most current guidelines from the American College of Physicians and NICE are recommended.

You can see the green is ones that in the Chou review had insufficient evidence or evidence of no effect, and the low strength of evidence is those that have some evidence of benefit, but it's not very convincing.

You can see there are gaps in this evidence, and there is a gap in what clinicians have to bring to bear on these issues.

I will say one other disclaimer, and that is this is one systematic review. This is not the state of the science on any of these conditions. This is a recent systematic review, and certainly further indicates the need for better evidence.

The final thing I will say is you will notice even where there is moderate strength of evidence, look to the left, exercise therapy is not something you can implement in your office that you can cover with any sort of specificity that you can recommend. Similarly, with acupuncture.

One of the things you will see in our targeted funding announcement is we are going to be asking for a much greater sense of specificity, so we know what is being proposed to be studied and why there is evidence that should be a good alternative.

In setting this up, we looked at ClinicalTrials.gov. There are 19 open or active trials. You can see the range of different activities they are looking at. Eight of these 19 are comparative effectiveness research, a number of them are head to head trials of medication. There

are some that are various combinations of therapy.

There is one that I bet is having no trouble recruiting, the third from the bottom, Cannabis versus Oxycodone. I bet they don't have recruitment problems.

None of these -- they are looking at various combinations but none of them are looking at optimal sequencing and few of these are evaluating the commonly used or recommended combinations.

Our proposal, and I will say the SOC did approve this proposal, I think, with a lot of enthusiasm, is what is the comparative effectiveness of combinations and/or sequences of non-invasive interventions for patients with non-specific, non-radicular chronic low back pain.

We are taking this approach by specifying the PICOT, and it's a little different than some of the targeted announcements we have done before where we have just gone to one question.

We are saying that we are interested in patients with chronic low back pain defined in one of two ways, and these are the ways they are usually

defined in the literature. We are interested in heterogeneity, treatment effects among these patient subgroups in whom there is a priority, either evidence of difference or something stakeholders have told us they believe there are potential moderators of treatment effects, or investigators can propose another important subgroup if they have an accompanying strong rationale.

We are not looking for data dredging, we are looking for priority indications that you would expect treatment modifications.

The intervention and comparators are combinations or sequences that are either in common use or have adequate evidence of efficacy or effectiveness, and we have called out ones that of interest but are not limited. We are not limited to these.

Active physical therapy modalities, complementary and innovative health, non-opioid pharmacologic interventions. We already have quite a bit of work going on in opioids, and opioids are not really recommended for chronic low back pain, so

we are specifically excluding opioids from this funding announcement.

Multidisciplinary/interdisciplinary rehabilitation programs.

As I said, the comparators, if they involve something like exercise therapy, acupuncture, or yoga, they need to be adequately operationalized, and the proposed operationalization must align with the available evidence, so you can't say you did a study over here and they used some exercise thing and then we are going to do exercise over here, but there is no connection between them.

We want to be sure because patients enter into back pain treatments from a variety of ways. They can come in through a chiropractor. They can come in through massage therapy. They can come in through their primary care doctor. We want to be sure that the combinations or sequences of interventions that are tested address actual clinical choices that would be faced by patients, caregivers, and clinicians in specific practice settings.

Otherwise, you could just have somebody taking an A and a B and throwing them together, and it is really not going to help.

We are asking for a minimum set of outcomes. I'll be talking to you more about moving towards asking for more core outcome measurement across our portfolio, because I think that is a smart way for us to go as funders.

Here, what we are doing is we are saying we are interested in at least a measurement of function, pain, quality of life, return to work or premorbid function, and health care utilization.

We are trying to make sure that we get the measures that meet the needs across a range of stakeholders, and we are asking for outcomes that are up to and beyond 12 months if possible.

We have set forth an amount of $50 million in total costs that we suggest be made available. This would fund somewhere around three to four studies at a total direct cost of $10 million a study, with a maximum project period of five years.

The SOC voted on this and approved it on

October 4, and I'm bringing it to you today. I'll turn it back over to Gray for discussion, questions, et cetera.

DR. NORQUIST: Let's open it up for discussion.

DR. COLLINS: Can I ask a question?

DR. NORQUIST: I'm sorry, Francis.

DR. COLLINS: I'm glad to see the creative aspect of the study, but I must be missing something because when I see you have listed four possible interventions but there are probably going to be others, and within those four, there are various options like acupuncture versus spinal manipulation.

It quickly adds up to a very large number of possibilities here in terms of what these interventions might be, making me wonder how will the potential very long list be shortened, and if you don't shorten it substantially, have sufficient power to actually know what works? I must be missing something here, because it seems like you have a huge number of options that would be on the table.

DR. WHITLOCK: I think it's a great question. We are asking that the potential options actually be things that have previous evidence of efficacy, are logical combinations or sequences in a specific practice setting, but we believe at this point in time, as you saw from the number of different treatments that are now in guidelines and the disconnect with the evidence that is available, that this is one of the situations where we need to see what comes back from the field because there is so much missing and there is no way to prioritize specific combinations or sequences at this point.

That is my answer. I think Leah and/or Christine or others that have worked on this may also want to add in.

MS. HOLE-MARSHALL: I think that is correct.

DR. COLLINS: Would you ask each applicant to pick just one sequence of interventions or are they going to be saying we are going to try six different ones, and you have two or three other applicants who are trying a different set. I'm just

worried about heterogeneity here.

DR. WHITLOCK: No, I understand. Just to be clear, at this point in time, we wouldn't necessarily have three different trials that would look at the very same thing. We're not necessarily going to have that.

If we do have the same measures, and one of the things we have talked about, I don't know how feasible it is, at least on the table is the idea that -- sorry. If we ask people to do a common set of measures, function, pain, quality of life, return to work or premorbid function, and health care utilization, between the time of the Board's decision to fund certain things and us awarding the contracts, we may be able to bring those all into common measurements, which would give us more power to work with the results even if there is some diversity.

DR. COLLINS: Would you consider adaptive trial designs?

DR. WHITLOCK: Certainly.

DR. COLLINS: Why couldn't PCORnet be an

applicant?

DR. WHITLOCK: Well, they could.

DR. NORQUIST: They could, of course.

DR. WHITLOCK: They could, absolutely. I think the other design that might be good is one of the smart designs, where you have a sequence and you are randomizing it as people fail. We are hoping by asking for sequences that people will bring the latest design approaches into play.

Christine?

DR. GOERTZ: Evelyn, are you planning to use the minimum dataset for chronic low back pain that the NIH's advisory panel recommended for the study of low back pain?

DR. WHITLOCK: Are you talking about outcome minimum dataset or the characteristics of the participants?

DR. GOERTZ: It actually included both.

DR. WHITLOCK: We have asked for some of the outcome measures that were called in that dataset. The participant requirements are pretty extensive. We have not incorporated that at this

point because they are quite extensive. I am happy to talk about that more.

If the Board approves this today, we would have until January to actually put the targeted funding announcement together, so we can work on that if that is something you think is important.

DR. GOERTZ: I do think it's important.

DR. NORQUIST: Gail?

MS. HUNT: Can I just ask why we need to make this a five-year study? If you're talking about getting an RFP out in January, and then usually it takes us a year before we award. That is 2018. Then you are talking about a five-year study.

DR. WHITLOCK: This is the maximum, and certainly -- I don't think, just to make a minor correction, if the award is made in January, we should be able to execute a contract within a matter of months. It doesn't take a year to make the awards.

MS. HUNT: No, it takes a year from when the RFP goes out.

DR. WHITLOCK: We have already put out --

I'm sorry, I beg your pardon. I'm thinking about the other one. Sorry. So many back pains, so little time. You're right. We can't fund this for a year. We can put in the PSA that we would be interested in shorter term studies if possible, but the reality is if it's a large study and a pragmatic trial, and this would be a fairly big study, it often takes a fair amount of time to accrue the patients.

It's just the nature of research, unfortunately. I'm not making excuses. I'm just saying it takes time. We can talk about that with people, but it is what they can actually manage.

DR. NORQUIST: Rick?

DR. KUNTZ: This is obviously a very important study. Are you going to stratify any of the structural aspects, like spondylolisthesis, things like that?

DR. WHITLOCK: I don't think spondylolisthesis will be in here because these are people with non-specific, non-radicular pain. If they are in there, it won't be because they are

diagnosed, it would be incidental. I don't know that we will have that information to do stratification.

Can you tell me differently? I'm not a spinal surgeon.

DR. KUNTZ: You are going to have a high percent of people that have spondylolisthesis. If you look at the most recent literature on stabilization, there is a lot of recent information, randomized trials published, about the different surgical/non-surgical interventions. Everybody will have an x-ray.

It just seems like it is sort of missing, that you don't have some kind of anatomical stratification based on the disorder.

DR. WHITLOCK: Let me look to my experts.

DR. GOERTZ: Actually, the guidelines right now, the current existing guidelines, don't call for x-rays in this particular case unless there is some sort of red flag. If I were doing this clinical trial, I might recommend there be a subset of people that have x-rays because I want to rule in and rule

out some pathology or contraindication to the treatment if it includes spinal manipulation, for instance. I would not blanketly assume everybody would be x-rayed, because that wouldn't necessarily be consistent with the standard of care.

DR. NORQUIST: Alicia?

DR. FERNANDEZ: Quick question, and maybe to Christine. I may not have understood this previously, I apologize for that. We're not saying that patients cannot be on opioids in order to enter the trial; right?

DR. GOERTZ: No. We're saying that one of the experimental conditions cannot be opioids versus something else or opioids and then in sequence with something else.

DR. FERNANDEZ: A person can be on opioids and be randomized?

DR. GOERTZ: Yes, that would be an inclusion/exclusion criterion. All we are saying is we don't want any more studies where it is an active comparator.

DR. FERNANDEZ: Great. I had the fear that

we wouldn't be able to recruit anyone.

DR. GOERTZ: That would be if they were still experiencing some level of quite significant pain.

DR. NORQUIST: Evelyn, we don't have any data on the most common intervention? I'm kind of thinking about what Francis was talking about. You could get a variety of different combinations, and then we will have to weigh the applications to decide which ones had the more important, if you will. We have $50 million. We may get a huge study with sequential analysis of something, and it is going to be $40 million.

Are the interventions they are proposing going to be more important than another -- listening to the prior panel and others, if we had some idea.

I was actually curious because I will tell you that one of the interventions which I see all the time used was not on your list, which is Gabapentin. It is used like water out there, quite honestly, for a lot of pain stuff. I didn't see that at all, and we have no good evidence about

whether -- I can tell you a lot of people are on it.

You may get that versus -- I don't know. I think it is going to be interesting, and we will have to deal with that, I guess, when we get the applications. We do need to a priori have some idea about which of the interventions we feel are the most commonly used, most -- we can't use cost, from a value or something, are the ones that are most important right now, the ones they are using the most. That should somehow get more weight.

I guess we're not giving a very specific question, we want to know whether X versus Y is right. I think we need to have some a priori sense of that or we could potentially get a bunch of applications with a variety of different mixes, and we are not sure which ones are really the most important, if you will, from a policy point of view or other kind of point of views.

So, just something to think about. Christine?

DR. GOERTZ: I think we want to be careful about doing that to some extent and perhaps leave it

to the investigative teams to do the justification for why their combination is most important.

For instance, a recent Gallup study showed that about 15 percent of people go to a chiropractor in any given year, only about one or two percent go to acupuncture. Yet, the evidence for acupuncture is at least as strong, perhaps a little stronger.

It's hard to know what to tether it to, so I think it is actually better for us to leave it up to the investigative team to build a convincing rationale for why they think their combination is the best.

DR. NORQUIST: Here's my concern. My concern is at the end of the day, what evidence can we use to make decisions about what we should pay for, so we get a trial of manipulation versus acupuncture, and whatever one comes out. Now we don't know whether some of these other very commonly used interventions, like Gabapentin, then we are back.

If somebody came in with a trial and said we're going to try -- I'm just making this up --

manipulation versus opioids and something and that didn't work, well, the next sequence up would then be acupuncture, and that might be of interest. Then we might be able to show something is more worthwhile.

I'm just worried about this multitude of combinations, I think what Francis was alluding to, where you could get one trial that is A versus B, and another one that is B versus, you know, you may not know at the end of the day what to really tell people, except on an one to one kind of thing.

DR. GOETZ: I'm not arguing with the complexity of the issue, just that if we make that decision, we will essentially be making stuff up. It's so difficult to --

DR. NORQUIST: I don't think we are making stuff up about what's the most prevalently used, if you will.

DR. GOERTZ: We could use what is most prevalent, but that does cause us to miss some things that might be important.

DR. WHITLOCK: Right, and even stakeholders

told us they were particularly interested in acupuncture, and I don't remember why exactly, but it depends on the perspectives.

Leah, did you want to add?

MS. HOLE-MARSHALL: Yes, just to say a couple of things. When the committee was called the PDC, we wrestled with back pain. It has been that long where really smart people have tried to come to a very specific question, and we have not been able to get there.

This was a different approach, and non-interventional, to try to get there. I don't believe we are going to see six sequential trials of things that have absolutely no evidence given the way it is structured that would pass and get a high quality merit review score. I'll allow that is a possibility.

With respect to whether or not we want to have comparators like opioids, the problem that we get into, one, we have a lot of studies with a specific focus on opioids right now, so I'm not sure we want to spend our money that way, and there are

many in the community that think things like opioids or Gabapentin are actually not useful at all.

So, having seen other studies of using those as a comparator group it isn't helpful to folks in the community who think that, and I think there are risks involved.

DR. WHITLOCK: This was meant to get at one area of back pain which is non-interventional, non-surgical approaches, and to see if we could get some comparators where you have patients and purchasers and employers all out there struggling with do I go to PT, do I go to acupuncture, do I go to a chiropractor, do I authorize 10 visits, do I authorize active physical therapy. What does CBP mean? Do I do that in conjunction with PT?

They are very common. As long as these researchers have engagement, which is an important part of our strategy, these common questions about whether to do some interventions together or sequences, I think, we will get, and then the question is do we want to delineate that up front when we have struggled for five years to do that and

haven't been successful. To me, that was the bottom line question.

DR. NORQUIST: Yes. I think you actually were arguing for some of the more common things at the end there, but I think we just need to be prepared for a situation where -- one of the things that was learned is we have not always gotten in from asking for requests, which is one of the reasons we are having conversations about whether we should be much more focused, because we haven't always gotten what we had hoped to get in.

We should have a Plan B, too, because if we are putting this level of money out on back pain and we don't get anything that we really think is good, what is our thought about where do we go at that point. I guess we go onto the next topic or something.

DR. WHITLOCK: I would say a couple of things. My sense of where the evidence is, and I haven't been here for the whole five years, but for the time I have been here, people cannot get any more specific than we have gotten. In fact, getting

to this level of specificity was an accomplishment.

The problem is back pain, chronic low back pain is very heterogeneous. Nobody knows how to really figure out what is going on. The treatments are very heterogeneous, and you access them through a whole bunch of different settings.

It's kind of a difficult situation to do very targeted research in. Because it has been one of your priority topics and many stakeholders told us it was important, I think PCORI could say well, because we aren't sure we can get a definitive study that is going to change the world, maybe we shouldn't contribute.

I think this is moving forward with the idea that this is such an important area that it is worth investing in and improving the science from a comparative effectiveness viewpoint. That is a Board decision. I think you can very well talk about that and decide it is not worth it.

I'll be honest. My belief is I don't think -- there may be some things where we really bring some incremental knowledge that will help some

people out of this research, but we're not going to have the answer at the end of this. There is a lot to be done.

DR. NORQUIST: Just to be clear, I wasn't arguing against doing something in back pain. I was arguing about being a little more focused on the question. Kathleen, and then Freda.

MS. TROEGER: Evelyn, thank you.

DR. NORQUIST: I see Bob Zwolak also.

MS. TROEGER: I agree this is an important area, and thank you for bringing it forward. I have a question that you may have answered in the PCOT outcomes portion, but it gets back to where there be a common set of definitions and criteria, particularly because this is non-surgical measuring, the pay/ time off, the absenteeism, pieces like that which are easier from my perspective to measure in surgical interventions and others than in chronic situations where pay/time off and other pieces may or may not be easily reflected in the EMR, and issues like that.

It puts a big burden on the participants to

record that data as well, if it is being collected prospectively.

DR. WHITLOCK: We had specified that we would look at health care utilization. This is a minimum. People can measure beyond this. We would look at return to work and premorbid function, so we wouldn't necessarily be looking at that particular pay/time off. Certainly, if people think it is important, but I think your point was it would be hard to measure in a non-surgical case.

MS. TROEGER: Not particularly like you would see in a surgical case, although return to premorbid function, can you lift this, can you function at your job.

DR. WHITLOCK: Right, and that is why we wanted the return to work or premorbid function, which also gets people who are retired.

DR. NORQUIST: Freda?

DR. LEWIS-HALL: I'm sorry I didn't follow more closely, but have we done any analytic, not on the current data but in datasets with predictive markers? I'm asking because there are a couple of

examples of using large systems where you know the outcome, so patients are hospitalized in the last 12 months, for example, and then you de-identify the data, you give it to mathematicians, not clinicians or researchers, and say can you develop an algorithm that is comporting with the patients going into the hospital, and then what are the predictors of those for the interventions.

Actually, a couple of studies that demonstrated some fairly good results, and it doesn't give you the answer to what you should do, it gives you the answer to what you should study and evaluate further.

Do we have anything like that in this space that we have used to hone up in, or could we maybe get more targeted?

DR. WHITLOCK: You're speaking my language, predictive analytics. You saw me put that stuff in there. Joe said he went to visit with the North American Spine Surgeons. Do you want to say what they said?

The bottom line, Freda, is I don't know

where we would get those data right now. It's a really interesting question.

DR. GOERTZ: Not exactly what you were asking, Freda, but there are several studies and PCORI has funded a couple of studies on risk predictors, leading from acute low back pain to chronic low back pain, which is what we are talking about here.

It is a risk prediction model. There are quite a few published studies on risk prediction models. It's not genomics. It tends to be psychosocial, expectations for recovery, whether or not they were given messages related to activation and what to expect in terms of back pain resolution.

There is quite a bit of literature, and we did include it in one of our systematic reviews on topic briefings, when we were trying to decide between the prevention of chronicity versus treatment of chronic individuals. We do have that information, but it is not derived from the same source you are suggesting.

DR. WHITLOCK: It's not actually on this

particular topic, which is treatment options for chronic low back pain and outcomes. It's the transition. I think the back surgeons were talking about being interested in predictive analytics for who does well with surgery. It's a little different.

I guess I don't know if we have a dataset that we could do that with. I think it is a really good question and interesting question. I'm not aware of a dataset.

DR. NORQUIST: Bob, and then Joe.

DR. ZWOLAK: Briefly, I'd like to say that SOC has struggled with this mightily, and we hashed many of these arguments that have come to the table today, dating back to the PDC. It is in fact, I think, why we purposely opened the lens a little bit in terms of making this proposal less specific rather than more specific.

There was some method to our approach here. I won't say method to our madness. Method to our approach. Potentially, science staff could work additionally in parallel to posting this to see if

we can come up with some more information by the time the LOIs arrive, not to dissuade any decisions, but to inform our decisions as we move forward. Those efforts could be done in parallel.

DR. NORQUIST: Joe?

DR. SELBY: First of all, it is true that the outgoing president of the North American Spine Society in his closing talk said predictive analytics is the future of back surgery, and that once the data are available, it will be the responsibility of back surgeons across the lands to have the courage to act on it. It was really quite a moving noteworthy talk. I was blown away.

As we were working through the back surgery/back pain question, which was another gigantic question to try to wrestle to the ground, one of the groups that visited us, and the North American Spine Surgeons did, the orthopedists, and the neurosurgeons separately, and one day the physical therapists came. They talked about the fact that there really was a sort of algorithm or sequence that exists in guidelines for people who

just entered the categorization of chronic low back pain.

That was the point at which this notion of an adaptive smart trial really came, I was just impressed by what they had to say.

I share Francis' concern to some extent. I know that we can't lay out the exact question or questions or the exact sequence. Do you think it would be possible to say we're not interested in just a treatment A versus treatment B here. There are too many treatment As and treatments Bs. We want you to give us a theory about a sequence backed up by evidence and linked to the present guidelines, and some question points along that sequence that we can test with randomization.

That would be a combination of a smart trial -- a smart trial is a type of adaptive trial, it depends on whether you respond to one. That way, we could get multiple answers out of the same study, and mimic real world practice better, and actually it might be easier to recruit to, too, because we are going to give you this sequence and see how you

do.

I would just say if we could think about that. We have a long history of leaving the final decision making up to the research community and then having sometimes mixed feelings about what we have to choose from, even when they are well designed studies.

I think if we could put the onus on the applicants to go that extra step and really make this an adaptive study that mimics practice and not just this versus that, we would be ahead.

DR. WHITLOCK: Great.

DR. NORQUIST: Christine, and then Ellen.

DR. GOERTZ: I think that sounds like a really fantastic idea. The problem is it is just not that easy, that sequence of events is just not as nailed down as we wish it was. The guidelines, there are not enough of them, they are not for enough various treatments that we are going to be studying, and I think to say we are interested in sequential treatments and we are interested in you actually provide a rationale for why you chose

those, that is all very doable.

To say it has to be tethered to existing guidelines or there has to be an evidence base for that sequence, that is too high of a bar.

DR. SELBY: Maybe the alternative would be that if you are really at the beginning of a sequence, if you are a patient at the beginning of a sequence, then that could be just a simple straightforward, step one would be head to head. After that, you would have a sequence.

Does that make sense? In other words, it wouldn't say there is a sequence, but you could allow two, even three initial approaches, and then at a point where they failed, you could still have two or three at that point.

I think we have to get more out of this, and something more definitive than this versus that, or we will be back.

DR. NORQUIST: Let me just interject because it reminds me of when we did the trial on depression, treatment resistant depression, some years ago, and we had a sequential approach. You

had to take one antidepressant, and if that didn't work -- there is no guideline, but we basically said okay, here's what the field believes at this point about this is rationally what we probably would consider next. We had three or four different steps.

People, if they didn't respond to the first would fall into the next, and then we would get a better sense about who might be responding.

You're not saying you couldn't do that. You're saying don't expect there is actually clear evidence about what step two would be, but someone could come in with such a proposal.

DR. GOERTZ: They could, it's just I think we need to make it clear we are not requiring an existing set in stone guideline or some evidence that sequence actually works, again, getting back to our request for preliminary evidence.

I agree with evidence that the different components have some effectiveness, but we don't really have research on how that preliminary evidence or how some kind of sequencing might work,

and it's possible that this community is not as aligned as the mental health community was in what that sequence might be, which is again why I think we need to express to the investigative team to justify their sequence.

DR. NORQUIST: I'm not sure we were that aligned. I would say there is a sequence that is going on in the real world, and I think in different places, and I think one could play that out.

What I think is I'm kind of like Joe, what I hate to do is have five or six head to head comparisons, and at the end, we just really don't know like what do we tell all these people who failed each one of these comparisons? Within a trial, you might be able to get a better sense, like a third responded, and another third responded, and then another third.

At the end of our trial with depression, we ended up with a third that didn't respond to anything, but we had two-thirds who actually got somewhere after a sequence. We wouldn't have predicted that necessarily at the beginning.

DR. GOERTZ: No, I'm not arguing with that. I can come up with three designs that I think would be fantastic along those lines. I think it just depends on how we set it up, and again, let the investigators justify.

DR. NORQUIST: I think we are allowing the investigators to justify. Ellen, and then Bob Jesse.

DR. SIGAL: I'm sorry. The adaptive trials are really important. There is a science to doing an adaptive trial properly, and for investigators that are not used to doing it, you have to be very careful about its design and how rigorous it is going to be. We do that at medical centers where they are used to doing a lot of these trials.

To get the right results on an adaptive trial, it really needs a lot of thought.

DR. NORQUIST: Bob?

DR. JESSE: In this emerging world of precision medicine, how do we do a trial like this that doesn't end up being a population study? This works for 30 percent of the people, but we find out

what works for which people, what markers, whether they are biomarkers --

DR. SELBY: That would be great; right?

DR. JESSE: Right.

DR. SELBY: That would be a good thing. That is the predictive analytics.

DR. JESSE: Right, but how do we ensure a trial gets designed --

DR. SELBY: I think we have to ask for both of these things. I think my point, Evelyn, was put some additional instructions in there for the investigators, so they don't come back to us with 14 different --

DR. WHITLOCK: Right. I think what I am hearing from this conversation, I'd like to respond and say we have said in this, and I'm thinking we should modify, it says "combinations and/or sequences." I think we should say "sequences," proven or commonly used treatments, alone or in combination, comparisons of those and sequences. I think we need to require sequences. That is what I am hearing everybody said.

They shouldn't be able to just get away with a couple of head to head things that we don't learn that much from. I think that is a really helpful outcome from this combination -- conversing.

DR. NORQUIST: Collaboration.

DR. WHITLOCK: Yes, collaboration. I think we could make that a requirement, and talk about the other designs that might help support that.

SPEAKER: Evelyn, you would allow combinations within the sequences; correct?

DR. WHITLOCK: Absolutely.

DR. NORQUIST: Absolutely; yes.

DR. WHITLOCK: You would not allow just A and B versus C and D. You want people to have somewhere to go if it doesn't work.

DR. NORQUIST: What we are approving is actually the money to be put toward this, the actual final RFA, you still have to develop.

DR. WHITLOCK: Right.

DR. NORQUIST: What I am asking now for is a motion to approve allocation at this point of $50 million for the development -- up to $50 million.

DR. JESSE: So move.

DR. BARKSDALE: Second.

DR. NORQUIST: We can do a hand raising. Francis, if you are still on, you can tell us yes, no, or abstaining.

DR. COLLINS: I think I have to abstain. I just don't feel comfortable we have a good idea of what we are doing here.

DR. NORQUIST: Okay. Francis abstains. All those in favor?

[Show of hands.]

DR. NORQUIST: Anybody opposed in the room?

[No response.]

DR. NORQUIST: Anybody abstaining in the room? Okay, Andy Bindman is abstaining. It passed.

That was our last session. I heard from Sue that we have no one in the room or online who would like to make a public comment, so we will not be initiating our public comment period. You are always welcome to go on our Web site and at Info@PCORI.org.

DR. SELBY: I want to thank everybody for a

great day. We're going to ask the Board members to stay for just a little while afterwards. We have a bit of a planning discussion. It shouldn't take too long. Everybody else can leave except the executive team and the Board members.

DR. NORQUIST: Just a reminder to people, all the information and recording of this will be on our Web site at PCORI.org.

That is it. Thanks, everybody.

[Whereupon, at 5:02 p.m., the meeting was adjourned.]