PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

BOARD OF GOVERNORS MEETING

Monday, April 30, 2018

The Wink Hotel
1143 New Hampshire Avenue NW
Washington, DC 20036

[Transcribed from PCORI teleconference.]
APPEARANCES:
BOARD OF GOVERNORS

Debra Barksdale, PhD, RN
Kerry Barnett, JD [Vice Chairperson]
Lawrence Becker
Francis Chesley, Jr., MD [For Gopal Khanna]
Francis Collins, MD, PhD
Allen Douma, MD [via telephone]
Alicia Fernandez, MD
Christine Goertz, DC, PhD
Leah Hole-Marshall, JD
Russell Howerton, MD
Gail Hunt
Harlan Krumholz, MD, SM
Richard E. Kuntz, MD, MSc
Sharon Levine, MD
Freda Lewis-Hall, MD
Barbara McNeil, MD, PhD
Grayson Norquist, MD, MSPH [Chairperson]
Ellen Sigal, PhD
Kathleen Troeger, MPH
Robert Zwolak, MD, PhD
AGENDA

1. Welcome, Call to Order and Roll Call
   Grayson Norquist, MD, MSPH, Board Chair

2. Consider for Approval:
   Minutes of March 20, 2018 Board Meeting

3. Executive Director’s Report and Q3 Dashboard Review
   Joe Selby, MD, MPH, Executive Director

4. Consider for Approval: Dissemination and Implementation – a new Implementation PFA concept
   Jean Slutsky, PA, MSPH, Chief Engagement and Dissemination Officer

5. Methodology Committee Update:
   Consider for approval:
   Request to adopt new standards
   Studies of Complex Interventions
   Data Management Plans

6. Lunch

7. Stakeholder Panel: Two patient organizations
   Bari Talente, JD, Executive Vice President, Advocacy, National Multiple Sclerosis Society
   Sohini Chowdhury, MA, Deputy Chief Executive Officer, The Michael J. Fox Foundation for Parkinson’s Research

Moderator: Gail Hunt, Board Member
AGENDA [Continued]

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Consider for Approval: Proposed Slates</td>
</tr>
<tr>
<td>Cycle 2 2017</td>
</tr>
<tr>
<td>Pragmatic Clinical Studies</td>
</tr>
<tr>
<td>Symptom Management for Patients with Advanced Illness</td>
</tr>
<tr>
<td>Medication-Assisted Treatment Delivery for Pregnant Women with Substance Use Disorders Involving Prescription Opioids and/or Heroin</td>
</tr>
<tr>
<td>Cycle 1 2017</td>
</tr>
<tr>
<td>Optimized Multidisciplinary Treatment Programs for Nonspecific Chronic Low Back Pain</td>
</tr>
<tr>
<td>9. Consider for Approval: Targeted PFA Development</td>
</tr>
<tr>
<td>Psychosocial Interventions with Office-Based Opioid Treatment</td>
</tr>
<tr>
<td>10. PCORnet Update:</td>
</tr>
<tr>
<td>ADAPTABLE Update</td>
</tr>
<tr>
<td>Searchable Tool</td>
</tr>
<tr>
<td>Dashboard Metrics</td>
</tr>
<tr>
<td>11. Consider for Approval: Proposed Slate for Cycle 2 2017</td>
</tr>
<tr>
<td>Partnerships to Conduct Research within PCORnet (PaCR) Awards</td>
</tr>
<tr>
<td>12. Public Comment</td>
</tr>
<tr>
<td>13. Wrap up and Adjournment</td>
</tr>
</tbody>
</table>
PROCEDINGS

[10:15 a.m.]

CHAIRMAN NORQUIST: All board members are present, with the following exceptions: Debra Barksdale, Richard Kuntz, Sharon Levine, and Freda Lewis-Hall, who were not able to join us. And Allen Douma is joining us by telephone today.

I want to remind everyone, disclosures of conflicts of interest for members of the board are publicly available on our website and are regulatorily updated. Members of the Board of Governors are reminded to update your conflict of interest disclosures if the information has changed. You can do this by contacting your staff representative.

If the board will deliberate or take actions on a matter that presents a conflict of interest for you, please let me know at the time so we can discuss how to address this. If you have questions about conflict of interest disclosures or recusals relating to you or others, please contact your staff representative.
All materials presented to the board for consideration today will be available during the webinar and then posted on our website. The webinar is being recorded, and the archive will also be posted within a day or so.

We have a scheduled public comment period today from 5:15 to 5:45 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 email us at info@PCORI.org, or provide input through our website.

Finally, a reminder: We're live-Tweeting today's activities on Twitter, and you can join the conversation with @PCORI.

So I think, Joe, unless you want to make comments now, we'll go ahead and do the first item on the minutes?

DR. SELBY: Yes.

CHAIRMAN NORQUIST: Okay. So we'll get the next slide. Before I do that, I just want to check. Allen, are you on the phone?
CHAIRMAN NORQUIST: Okay. So I guess Allen is not on yet. When he comes on -- oh, I have the control. There we go. Okay. That's just the agenda.

Okay. So the first item is approval of the minutes from our March 20th board meeting. So I need a motion.

DR. ZWOLAK: So move.

CHAIRMAN NORQUIST: Yes, Bob Zwolak.

DR. HOWERTON: Second.

CHAIRMAN NORQUIST: And then second, Russell. Okay. So is there any discussion or any changes to the minute at this point?

[No response.]

CHAIRMAN NORQUIST: Okay. If not, I just need a voice vote. All those in favor, aye.

[Ayes.]

CHAIRMAN NORQUIST: Anybody opposed?

[No response.]

CHAIRMAN NORQUIST: And anybody abstaining?

[No response.]
CHAIRMAN NORQUIST: Okay. So let's see. Joe, I think it's time for you to give us an executive director's report.

DR. SELBY: Okay. Thank you, Gray. Good morning, everyone. I'll be relatively brief today; just a few items. We have an action-packed agenda with a lot of approvals and adoptions.

But there are a few pieces of news that I wanted to share. And the first one is, as some of you have already heard, the long-awaited GAO report of 2017/2018 that was mandated by Congress is now complete and is published. And the good news, the really very good news, is that it was a very straightforward publication with no recommendations, no deficiencies cited, no recommendations for improvements.

These are just three quotes that we were happy to see in the report, that we have done what we said we were to do, which was to primarily commit our funds for research and data capacity-building efforts; and that awards for dissemination and implementation of findings were, and particularly in
2017, still quite limited, as most research was still underway. As you all know, awards for dissemination are on the increase now, and implementation are on the increase, as our results mount. But this was very accurate for the time, which was through 2017, that they reported on.

The second was that they interviewed a number of stakeholder organizations, and this is a comment specifically about PCORnet, that a majority of stakeholders -- or that the stakeholders generally agreed that PCORnet does offer value by improving the data available to conduct comparative effectiveness research.

And the last one was something that we have been saying ourselves since 2012. But it was good to see them say explicitly and of their own accord that PCORI research awards have increasingly focused on conditions that impose a substantial health or financial burden on patients in the healthcare system.

So this is a stepping stone, something that was mandated on the way to consideration of
reauthorization. And this has passed, and the good
news is that we did very well in the report, and
move on to other aspects of the reauthorization
discussion.

At your table, I think -- let's just see.

It made it. Okay. This is a new communication that
I would recommend. It can also be found on our
website. You can download it and print out as many
copies as you wish. But this was a suggestion that
came from a stakeholder friend of PCORI's. She
said, "Do you have anything that talks about PCORI's
greatest hits?

So this is PCORI's greatest hits, volume 1,
and it's brief summaries, with links, to 11 studies,
11 CER studies, published CER results, which I
think, taken as a whole, really give anyone that
you'd hand it to a sense of the kind of research
PCORI does.

Now, I will say that these are all the
product of the early more or less investigator-
initiated, investigators with patients-initiated,
broad awards, so smaller studies. But there are
some very impressive findings, the kind we hope and
expect there will be many more of. And they make
the case that this type of research does very often
pointe to ways to improve the quality of care.

And not infrequently, it points at the same
time to ways that can lead to reductions in the cost
of care. So even though these are not yet our
larger targeted or more focused awards, simply
putting patients and their interests, physicians and
their interests, into the mix of the research
questions asked and studied, begins to give you a
principle of research that's distinctive and that I
think we can all be quite proud of.

So as I said, go to the website and
download as many copies as you'd like, and hand them
out if you're giving a talk or otherwise talking to
people interested in PCORI.

So the next topic, and again this will be
relatively brief, but I want to tell you that we are
moving ahead with parts of the strategic plan update
that we discussed in February and again in March at
our board meeting in March.
And this is the proposal to address stakeholder needs in relation to new therapeutics and new technologies. So PCORI recognizes, and we have actually been criticized, for not being more active in the area of new therapeutics or new technologies.

Not only do they arrive on the scene without a lot of evidence, but oftentimes they are high-cost interventions as well. So for a lot of reasons, patients and physicians, delivery systems, and health plans have questions about these. And the criticism was that we were not jumping on these as quickly as we should.

And we don't actually disagree entirely with that. We've encountered real barriers to launching studies of new technologies immediately. And we've also encountered the fact that CER studies take years to complete, even if you would start them the day that a new product was approved.

So the logic here is that there must -- if we're going to do something, it won't only be launching new five-year studies. And so this is the
first part of that, which is establishing a Horizon Scanning program.

Now, Horizon Scanning is something that has been done in the U.S. previously but is not currently being done and freely available to the public. So we are committing to launching, to identifying, a vendor to conduct Horizon Scanning to market new technologies and therapeutics in healthcare before -- in the years before they're approved.

This kind of Horizon Scanning is -- our payers stakeholders, patients, clinicians, tell us that it's very valuable because it helps them anticipate new questions that they're going to have to address, new policies they're going to have to set.

Building a framework for Horizon Scanning requires working with all stakeholders to decide on how one identifies those technologies and therapeutics that have the highest potential for impact, both on outcomes and costs of care, early on and focusing on them. And Horizon Scanning is also
a part of a topic-generation process, which we also want to revitalize as part of our strategic plan update. So one of the things Horizon Scanning does is points us early on to research questions that indeed we could launch studies of.

In addition to the Horizon Scanning, we want to link the findings from the scans to other information that is available on emerging therapeutics and technologies. So we are beginning to generate new products that can provide information, timely information, for patients, clinicians, and payers in lieu of completed comparative effectiveness research studies.

So certainly not a substitute. But reports that include topic briefs, evidence mapping, and more in-depth evidence synthesis when there is enough evidence to synthesize are a part of what PCORI can bring to decision-makers. This is pre-research type of summaries, but they are intended to meet, as well as one can at this time, the information needs, and also to point to ways toward more definitive research.
We are vetting the content of this with stakeholders. We have an upcoming meeting with payers in July where we will go through the proposed packet. We'll focus on particularly drawing out patient-centered outcomes that may have been either -- there may be evidence on them or they may have been overlooked, and it's important to point out that they've been overlooked -- disruptions in care, redundant care, and comparisons that are going to need to be addressed in order to accurately measure value.

The desire to measure value is there on day one. The evidence to measure it accurately may not be, also, to point out any ongoing studies that stakeholders need to be aware of, including the patients populations that are being studied and the settings where they're being studied.

We think that by tying these products together and tying them to future research priorities as well enhances the value to decision-makers and builds the pressure for the kind of research that PCORI can fund and generate.
So next steps in this area: We have already been generating evidence updates on topics that we may have done studies of or where we recognize that there's a need for an updated systemic review.

So the next evidence update coming out is one on treatments for PTSD. We are currently developing our very first briefs on new and emerging technologies, and one is on CRISPR technologies and one is on CAR-T. And these are expected in six months.

The Horizon Scanning program will be awarded by the end of 2018. We are working and will be back with you to discuss further ways that we can revitalize our topic in research question generation and priority-setting and refinement, starting with Horizon Scanning.

And the last is that we've held consultations with patients and clinicians in January and February of this year, also with payers during that interval. And in June and July, we will be back with patients and payers again to discuss
what's most valuable in these kinds of packets and summaries of evidence around new therapies, new technologies.

CHAIRMAN NORQUIST: Hang on a minute, Joe.

I think Ellen wants to ask you on this last --

DR. SIGAL: Well, I have about 3,000 questions, which we don't have time for. But I'm a little confused about this on intent on Horizon Scanning and exactly what you mean. So it's CAR-T. We now have two FDA-approved therapies on it. We have now the CMS new genomic, with the foundation medicine. And we have a tremendous amount going on in the field.

But we don't have a lot of these LDTs and a lot of these tests that are not validated or not FDA-approved. A lot of discussion on whether they should be or not and whether they're measuring the right thing. And just as an example, we did a survey on two FDA-approved tests for ALK and for EGFR, where there are two FDA-approved tests. And what we found, the good news is that patients were being tested. The bad news is 70 percent were not
using that test.

So when you talk about does that mean the other tests are good or bad, I don't know. But most of these platforms are not -- they're not CAP or CLIA. So we need a little bit more specificity on exactly what you're trying to get at on this because there's great confusion, and frankly, great debate in the community on what needs to be done.

And if you go to -- there's no cancer patient today that will even to a clinic that won't be tested. But are these tests good? Are they not? Are they validated? When you're making clinical decisions, that's a big deal. So I just don't understand the department of exactly what the Horizon Scanning means and what we're going to do with it and what the criteria would be.

DR. SELBY: Right. Well, I think, as you say, because CAR-T and CRISPR are already here, so to speak, Horizon Scanning may be less accurate than the topic summaries, the summary briefs, and other syntheses of any kind of evidence.

Those two topics came to us in
conversations with stakeholder groups. So that's how we got to them. They are brand new. Not a lot if known about them except that they are transformative and costly. And so that's how we got to them.

You make an excellent point, Ellen. And I know you think about this a lot. And that is, there's a huge dearth of evidence about the diagnostic testing that goes with newer targeted, often, therapies. And that may be an excellent third topic for one of these summaries.

And my question is always: What kind of a study could help here? Is there a comparative effectiveness question at this point that could be asked around diagnostic testing? Because I know that it is a problem for clinicians and payers and patients.

DR. SIGAL: Again, there isn't enough time to go into all of this now. And there is a lot we can and I believe we should do. With my conversations with CMS, they talked about patient-informed decision-making on it because patients
assume every test they have is valid.

But specifically with CAR-T, you have ICER and other people that have done a lot of work on this. It's early, so there may be other things we can look at that perhaps are in the clinic today that aren't -- that is not so easy, and criteria that patients should use what we should use.

So this is a big, big topic. And I agree it's really important. But there is chaos and not a whole lot of agreement in the community on exactly how this goes forward. And payers are confused as well.

DR. SELBY: My hunch is that as we produce the first ones, people are going to appreciate that there are, as you say, lots of other questions where they would be useful as well.

And it's something we did not think of so much in the early days of PCORI: What can PCORI do other than launch CER studies? We're now thinking of it on a daily basis, and I think the answer is, there's a lot.

And you mentioned ICER and others who would
do value assessments or cost effectiveness assessments. We obviously don't do that. But we can help be very clear about where the evidence gaps are that those who do cost effectiveness assessments actually need before they can do them accurately.

CHAIRMAN NORQUIST: Barbara?

DR. McNEIL: Joe, thanks. I think this is a great idea. I wonder if, to get around something Ellen mentioned, I wonder if you could potentially reformulate what you said in the following way and say something like, "PCORI is interested in knowing what people are thinking about that's going to hit the screens in 18 months or 24 months." And that's clearly not CAR-T. That's here already. So there are a bunch of things that -- you'd have to really do a lot of looking to find them.

And then the second would be, of the things that we know about that are on the front page of the Times or the Wall Street Journal, what can we do? And this gets at some of the genetic abnormalities and their potential translations into diagnostic tests. Which of those can we actually study?
So it's really a two-pronged issue. It's what do people develop in the lab that's going to hit us in six months? And then given the things that are here that don't have enough data, what can we do to study them?

I think if we were to put on a newsletter emerging technologies, wow, CAR-T, people would say, "We've known about that for a year." And it wouldn't be quite as dramatic as saying, "That's been around. We're going to try and do something about it."

CHAIRMAN NORQUIST: Kerry?

MR. BARNETT: Yeah. I'd just like to take -- and first of all, thank you, Joe. And I want to just take this in a potentially little different direction, which is that I believe what's needed is an organization that funds the validation and evaluation of new products that are being pushed to the public.

So we're in a DIY approach now to the way in which things are going to be done, and it's growing quickly. And there's a lot of decision
support, testing, a whole range of things that are being done for the public, where there's a lot of uncertainty about the quality of the studies. It's a comparative effectiveness of sorts, but it really is an investigation as to what people can trust, whether the information's actionable.

And the FDA is beginning to focus a bit on digital health products. But on the consumer side, if it's just providing information, it's falling outside of a lot of the scope that's being defined. And the question really is, with many of the emerging technologies that are being targeted for consumers, whether that's -- anything from genetic analysis to any sort of decision support, particularly -- whether it falls inside or outside of the FDA. The question is, what's the value for individuals? How could it be used?

I think that's a really ripe area for us. We've so far been focusing on how we provide evidence that clinicians would work with patients to help use in order to guide decision-making. But increasingly, people are being marketed directly
with a wide range of products.

And for us, that might be a very interesting place to go, to provide comparative effectiveness information, and to help consumers be able to make choices about these options increasingly available to them.

DR. SELBY: Right. And some of them are an order of magnitude more complicated, probably, than things before, like this notion of genetic testing of tumors and the fact that not all labs are the same. That was a tough question to talk about how you would communicate to patients and clinicians.

But thank you.

Yes, I think you guys are seeing it the way we do, that there's a lot of information as new technologies become available. Whether for an individual patient this makes sense is still an open question. A lot of these technologies have had relatively little clinical vetting before their approval. So a lot of room for the kind of real world or post-approval research that we fund.

Okay. Thanks. So the last topic, I think,
for this morning is something that I really -- I want you to be aware of. I want everyone to be aware of this because it's quite interesting.

We, in our efforts to evaluate PCORI's research portfolio and our impact, several of you -- I'm thinking of particularly Bob and I think Gail, too -- have been involved in our evaluation work over the years, and Michael Lauer, nodding his head, as well.

And we've always known that to a certain extent, you cannot really evaluate PCORI's products thorough unless you have a comparator. Since we do what we do for everything, we don't randomize engagement. We don't randomize patient centeredness. We don't randomize the type of reviews we have. We don't randomize the requirements to have stakeholders on the research team.

So in the last six to nine months, our evaluation and analysis department, in collaboration with our Evaluation Committee that includes those board members, has refined the idea that indeed we
could do a comparison. And the logical comparison, the one and only logical comparison, in the U.S. is to the NIH and to their portfolio, in part because the NIH is very transparent about their research portfolio.

So we can gather data on their research portfolio that’s very comparable to the data we have on our own. We can gather some elements of data from sources like ClinicalTrials.gov, where we can actually gather information on our portfolio and theirs from the very first source.

NIH, obviously their main mission is not to conduct comparative effectiveness research, but they certainly do fund comparative effectiveness research. They tag it as comparative effectiveness research. And we can look at it and evaluate whether to include it or not in a comparison with our portfolio.

So I want to say, in addition to commenting on the transparency of NIH, just to say that Mike has been very helpful in helping us think through this comparison, and Francis is aware of it and very
supportive of it, supportive of these kinds of comparisons in general and of this one in particular.

So our E&A department has laid out an evaluation strategy where we will compare the comparative effectiveness research studies we've funded with those that are funded by the NIH. And there are four levels of the comparison.

The first level is just the portfolio characteristics, the types of interventions, the conditions that are studied, the outcomes that are measures. You can imagine that these could easily differ between the NIH and PCORI.

And not to say that the findings in one group are "better" than in the other group, but they very likely will be different, and this will be of great interest -- whether we are proportionally studying different conditions using different interventions, selecting different or different numbers of outcomes, all important.

The second is also descriptive, and that is of the principal investigators and their
institutions and the characteristics of those. So the disciplines, clinical versus PhD disciplines, the specialties; the years of experience out of graduate school; the institutions, whether they are academic centers or private research entities, or other sites, is a second type of descriptive comparison.

The third gets to issues of study efficiency. And this is recruitment rates, retention rates, and the need to change the primary completion date, whether the study ultimately reached the sample size that it stated on ClinicalTrials.gov that it was aiming for.

And the fourth would be beginning to look at the impact of the studies using altmetrics, which you're increasingly familiar with, as am I, and in more typical citations, bibliometrics, a little bit later on.

So I'm not going to go into this or belabor it. But E&A has developed pretty extensive inclusion criteria, both for our studies and for those that matched NIH. And my understanding is
that we have upwards of 300 studies in each bin. And they are studies from 2013 through 2016, so they will have information today about all the descriptive information. And soon they will have investigation about the success of recruitment as well.

MS. HOLE-MARSHALL: Joe?

DR. SELBY: Yes, Leah?

MS. HOLE-MARSHALL: In terms of what you're comparing for the portfolio, it would be interesting, at least from my perspective, to understand the study design or rigor to what methods were used for it as well.

DR. SELBY: Yes. Do you mean, for example -- so we will certainly have study design. Are you thinking about, for example did they adhere to methodology standards? That's an interesting one, and I have heard it mentioned before. I can't say with certainty whether it's doable. It sounds like to review 400 projects from NIH would be challenging.

MS. HOLE-MARSHALL: There might just be a
couple of standards that the Methodology Committee could recommend --

DR. SELBY: That's a very good through.

MS. HOLE-MARSHALL: -- or a criteria that would be a proxy for some of that.

CHAIRMAN NORQUIST: Yeah. Like ones that may not be commonly followed or something? I mean, Robin, I guess your group could think about that. That's probably not a bad idea.

CHAIRMAN NORQUIST: Barbara?

DR. McNEIL: So I guess Mike could answer this better. So Joe, you said you have 300 common studies in each category. So would that mean that there are 300 randomized trials in our group and 300 randomized trials in the NIH group?

DR. SELBY: They aren't all randomized trials, Barbara.

DR. McNEIL: So are they matched? That's what I thought was just being asked because it would be hard to compare an observational trial with a randomized trial.

DR. SELBY: We may have to do some of the
analyses in strata of just the --

DR. McNEIL: Okay. That's what I was asking.

DR. SELBY: -- just the trials. I agree. Certainly things like recruitment won't be real relevant in secondary data analysis. And some of ours are, and I imagine some of NIH's are, too.

Okay. So these are just some of the characteristics that we will take a look at. I won't belabor it.

So that's the report, and now we go to the rest of the day's agenda. We have -- almost every item is either an approval or an adoption item. We have a new -- consistent with where we are in our history, it's really time to focus more attention on dissemination and implementation, and Jean's going to present a proposal for that.

Robin's going to give her report, and great news that we have a set of new standards for adoption. They've been through the public comment period, revised, and ready for adoption.

We have a visit by two large patient
stakeholder organizations, the National Multiple Sclerosis Society and the Michael J. Fox Foundation, for lunch in the 1:00 hour.

We then have, from Evelyn and the Selection Committee, pragmatic clinical studies and targeted awards. We have a new targeted PFA development for your approval related to psychosocial interventions in office-based medication-assisted treatment.

And then we have a substantial update on PCORnet, and including, at the end of that, approval of some limited competition studies that were conducted within PCORnet called PaCR awards. So a full day with decisions at every turn.

And now I want to take a minute -- there's Evelyn behind me. The lady pictured here is Dr. Evelyn Whitlock, who announced to us and to the board close to a month ago now that in June she will be stepping down as the chief science officer. She's been in that role for well over two years, and I think by all accounts has really helped to transform many of the ways for the good, many of the ways that we develop our funding announcements and
manage our portfolio.

So Evelyn just brought a world of expertise. She brought passion. She brought real skills, I think, at building consensus on the committees that she helped to lead and staff, namely, the SOC Committee, the Selection Committee, and the Methodology Committee.

We've learned a lot from her. I'm very hopeful that we will find ways to keep working with Evelyn and so that we can continue learning a lot from her. She started a lot of new activities which I think are really right at the heart of what patient-centered care is about.

And those include the notions of -- I'll use this term, having been advised that the Methodology Committee doesn't recommend it; I use it -- but predictive analytics, how you push data to give more information for individual patients, how you bring studies together to do IPD meta-analysis with the same goal?

So we hope to continue working with Evelyn. But I just want to say personally to Evelyn how much
I've enjoyed the chance to work with her and how much I've appreciated and how much I've learned from her. And I suspect a few others on the board may have comments in that vein as well.

CHAIRMAN NORQUIST: Yeah. Let me just --

[Applause.]

CHAIRMAN NORQUIST: Yeah. Evelyn, I think Joe has said a lot, and I want to say also our thanks, particularly from the board, for all the great work you've done. And I do hope that there will be some opportunity to continue some of that, yeah. I know you're looking forward to probably being back on a different coast than on the East Coast, and a better climate, perhaps. All right. Thanks.

Bob?

DR. ZWOLAK: I can't let this opportunity go by. On behalf of the Science Oversight Committee, I simply want to say that Evelyn was an enormous breath of creative fresh air. She helped us organize our thoughts. She helped us move forward. She introduced new concepts of scientific
endeavor. And it's been a fabulous two years, and we will miss you immensely.

CHAIRMAN NORQUIST: And Christine and then Robin.

DR. GOERTZ: Thank you. I also wanted to thank you, Evelyn, for the tremendous amount of work you did with the Selection Committee. It is a daunting task to be making recommendations to the board about the awards that we fund, and your work in helping us develop, better develop, our processes and to streamline and bring a greater level of consistency to the presentations, and just -- I can't even begin to describe the difference that you made in our ability to thoughtfully consider all grants presented before us and to make sure that we're making the appropriate recommendations to the board.

So thank you so much. And we will miss you a great deal, and I personally will miss you also.

MS. NEWHOUSE: Yeah. I would just say Evelyn has the ability to be able to take some very complex issues and narrow them down and understand
what the PCORI role is. And we really enjoyed the way we've been linked to some of the PCORI priorities through Evelyn.

And she really has depth in methods expertise, so she's really helped us to think innovatively, to advance our thinking, and we've already started to think about ways that we can understand the portfolio and advance methods.

And she's just been a wonderful partner with the Methodology Committee, and we're going to miss her desperately.

CHAIRMAN NORQUIST: And I think we'll be hearing from Evelyn this afternoon on a number of other issues.

So Joe, anything else?

DR. SELBY: Yes. Yeah, we will be hearing from Evelyn, some of the final products, I guess, of the work she's done with the SOC and Selection Committee. And for those of us who go to dinner tonight, we will save some of the more humorous comments for then.

Let's see here.
CHAIRMAN NORQUIST: Is that it?

DR. SELBY: That is it for me, Gray. Back to you.

CHAIRMAN NORQUIST: So let me just check before we move on. I think Allen Douma was going to join us by phone. Allen, are you on?

[No response.]

CHAIRMAN NORQUIST: Okay. And then I also see that Steve Goodman may join us by phone. Steve?

[No response.]

CHAIRMAN NORQUIST: Okay. Maybe it's still too early for them.

Okay. So the next item on our agenda -- we're a little bit ahead, but maybe we'll have -- always good to be a little bit ahead -- is this proposal for an implementation funding proposal. Larry, you and Jean were going to present this. I don't know what order.

MR. BECKER: Yeah. Thank you. So I'm pleased to represent EDIC, the Engagement, Dissemination, and Implementation Committee, and Deborah, who is both physically and mentally
exhausted because she has a house full of guests this weekend; her daughter got married. So that's why she's not here. I guess that's an okay excuse. Right?

Okay. So the EDIC --

SPEAKER: [Off microphone.]

[Laughter.]

MR. BECKER: Well. So the EDIC has approved a new implementation PCORI funding announcement to go forward for the full board approval. And as you know, PCORI is entering a really exciting time. We've worked now for the last eight years on our investments into research, and we're producing lots of results, and there's starting to be a cascade, a tidal wave, hopefully, that can help realize our mandate to assist patients, clinicians, purchasers, policy-makers, in making informed health decisions.

So Jean's going to talk about in a minute the innovative. What she is going to talk about is targeted to implementation of PCORI's most major research findings, and is meant to coincide with the
release of those findings from the targeted studies, the pragmatic studies, and groups of studies on related topics and questions, so that we can actually see that these things come to fruition.

So the EDIC met a few weeks back, and we're really enthusiastic and excited about this opportunity. And I'll just turn it over to Jean and fill you in on the details. Thanks, Jean.

MS. SLUTSKY: Thank you. Good morning, everyone. I'm bound to screw this up, so -- ah, okay. So far so good.

So I won't read you this. You've seen this slide a million times, as has the public, which speaks to PCORI's mandate and our mandate for dissemination of research findings along with AHRQ.

And so this proposed funding announcement is really intended to heighten awareness of the results of PCORI-funded research and advancing efforts to put these findings into practice as well as improving healthcare delivery and health outcomes. And this is consistent with the dissemination and implementation program within
PCORI.

And just as a reminder, PCORI has three streams of dissemination and implementation activities from evidence from our research. The first, that you approved a while back, is the limited competition, implementation of PCORI-funded results. And this is really an initial step to get our research into practice. These are relatively small awards. They're also tied to the submission of a draft final research report as they go into our peer review process, which is mandated in our authorizing legislation.

The budget for this is about 9 million total funding in any given year. Up till now we've made about $6.1 million total investments, and we've completed five limited competition funding cycles and funded 12 projects in 21 states. Remarkably, these awards are split almost equally amongst all the portfolios, the research portfolios, including methodology, in PCORI's funding portfolio.

The second was actually approved by the board a little less than a year ago, which is a
targeted funding announcement for implementation of effective shared decision-making approaches. As you know, PCORI has a very large portfolio of shared decision-making tools. There's much less evidence and work done on the implementation of shared decision-making within the flow of clinical care.

And so this activity is intended to promote the implementation and systemic update of shared decision-making in practice settings. And these can be those that are previously studied at PCORI, or existing effective shared decision-making strategies that are not PCORI-funded. And that was something that you all were very adamant about, that this be an open competition.

And then the third component of our dissemination activities are the Gene Washington Engagement Awards. And these are really targeted toward organizations and communities that can propose meaningful documentation projects to spread awareness and increase knowledge or new evidence.

It's really intended to help communities, organizations, and individuals work together to get
things ready to disseminate and implement. This budget is about 20.5 million per year, and I neglected to say that implementation or shared decision-making is about 6.5 to 8 million total funding available per year. And in June we'll be bringing our recommendations for the first awards under the implementation of shared decision-making.

I wanted to show you the schematic of PCORI dissemination and implementation activities because with all the different things that we're doing, it's hard to put it in a cohesive whole. So as you look under PCORI evidence updates, which Joe alluded to, these are activities that are intended to be at the very beginning of the dissemination and implementation activity, including building capacity for dissemination for communities and diverse partners.

So really trying to get into communities and get into organizations that need a little capacity-building to start to work in dissemination. It also is a program of conference support, so we split those out separately.
And then looking at dissemination activities to bring results to audiences, we'll have a strong interest in using them, really priming the pump so that we make sure that we're targeting activities to payers, clinicians, patients, communities, and purchasers.

And then implementation activities, which gets at more of the distal end. And so you'll see up in red there, this is the new proposed targeted funding announcement, which is geared more toward implementation and those research results that have the most likelihood of having a large impact because of either their size or the direction of their findings. And these are intended really to have a large impact. And you'll see the other activities I previously told you about.

And underpinning this is our relationship with AHRQ, where we collaborate around nomination of a topic for AHRQ to consider for documentation and implementation. We have about five topics that we've nominated to AHRQ. And we recently held a pretty exciting stakeholder planning meeting around
one topic, around anti-coagulation for atrial fibrillation, last week, looking at activities that could be done to implement those findings into clinical practice.

So just to give you a background -- you know this, particularly the SOC and the Selection Committee -- that we've made research investments in a lot of high-impact research topics through our targeted funding announcements, our pragmatic clinical studies program, and the PCORnet demonstration studies.

We also have some broad or investigator-initiated -- totally investigator-initiated -- activities that are looking to be likely to produce some very strong research results. And they reflect priorities that were developed through a pretty systemic topic generation and research prioritization process that included close collaboration with stakeholders.

So between 2018 and 2022, we expect approximately 90 studies funded under these mechanisms we'll produce findings. And these
studies actually represent a large amount of money in our total PCORI investment, about $800 million. So the purpose of this proposed implementation funding announcement is to support projects that facilitate the update of peer review clinical comparative effectiveness research from our most major research investments.

And as I said, we expect these to be from the targeted funding announcements, pragmatic clinical studies, and the PCORnet demonstration studies. But we do expect there'll be findings from our broad studies that have the strong potential for impact. That may also be a focus of implementation for this funding announcement.

And then we are proposing, through a broad call for proposals, to engage and draw on the expertise, creativity, and capacity of a large and highly diverse pool of applicants and implementers, and in service of implementing these important findings. So we really want this to be a broad pool of applicants and a very diverse pool.

And the end goal of this, of course, is
promoting the undertake of peer review findings from high-impact PCORI-funded studies at the point of care or in other decision settings.

So this next slide is actually something that might be easier for you to read in your book. But it really just shows the trajectory of when we are projecting to get findings from the types of studies that I mentioned. So the very beginning will be in 2018, and then ramping up through 2022.

So eligible evidence for implementation in this funding announcement includes published peer-reviewed evidence emerging from areas of major PCORI investments, and I've already highlighted these.

And each release of the funding announcement will identify selected areas from among the eligible research, so if you will, a sort of a special emphasis, knowing that we will have information that comes out of our peer review process as well as the published literature, including commentaries and editorials that accompany publications.

And this flexibility will allow us to
promote collaboration and avoid duplication with AHRQ. AHRC selects PCORI CER findings; it's the focus of its own implementation activities. This will allow us to collaborate and have a much larger impact than if we were to fund this in isolation.

So this proposed funding announcement will extend and compliment existing dissemination and implementation funding initiatives by providing a mechanism for PCORI to focus on findings from very high-profile, high-priority, and high-impact initiatives.

It'll attract a larger and broader pool of applicants, including implementation experts and diverse stakeholder partners, such as different organizations and communities, regions, and states, through an open competition.

And it will provide the opportunity to propose larger implementation projects that could be funded otherwise, and to promote the uptake and integration of these findings.

So just to give you an overview of where we are, thinking of the funding announcement overview,
the funding announcement release would be cycle 3, 2018, which is this coming October. And the first awards would be funded in the summer 2019.

As you know, this is an escalated review process, and for this I really want to thank our colleagues in merit review for working with my program staff to recognize that we want to decrease the time from the publication of findings to actually working to get them implemented and awarded. So we all, as I want to say, took a little bit of a hit and shortened the time that we have to do merit review, and program to go back to applicants with questions.

The maximum project period would be three years. The funds available would be up to $10 million per cycle, and we're expecting two cycles per year. And the funds available would be adjusted in line with increasing availability of evidence from major PCORI research investments.

This is proposed as an open competition. Applicants may or may not have been previous recipients of PCORI awards. And the standard
organization eligibility criteria for PCORI awards apply.

And so the implementation projects are expected to incorporate active strategies that will lead to the uptake and integration of PCORI evidence in real world practice settings. And they're intended to target specific end users, who are committed and motivated to use the evidence, so have some -- I hate this "skin in the game; I have to think of a baseball analogy rather than football.

And then demonstrate commitment and buy-in from proposed implementation sites to improve healthcare quality and a willingness to invest in the evidence being implemented such that they provide a supportive context and culture for undertaking the proposed project.

And work with regional and national stakeholder organizations who are positioned to extend the impact of PCORI evidence to broader end use.

And then we expect them to be guided by an established conceptual model or framework for
dissemination and implementation; and wherever possible, by evidence regarding the effective strategies for implementing evidence-based practices and interventions in different settings.

And then to address the adoption -- adaptation, excuse me -- of findings to facilitate uptake in the proposed settings, scale-up in order to reach larger numbers, and scale-out, to reach broader audience, as applicable.

And then include rigorous evaluation efforts to plan that document. EDIC felt very strongly about this in all of the projects that we fund through all the different mechanisms I mentioned. So there needs to be a rigorous evaluation that documents successful execution of the implementation strategy and the impact of implementation projects on outcomes, including measures of behavior change, healthcare utilization impacts, and impacts on healthy outcomes, as feasible and appropriate within the project scope.

So again, this is the timeline and where we are in the timeline. The EDIC endorsed bringing
this targeted funding announcement forward to the full board of governors on March 13th of this year. Today we're asking for a vote of the board of governors. If you approve it, we'll begin the formal PFA development and release the funding announcement in September, and have an applicant town hall in October.

Our letters of intent would be due for the first cycle in November. The application deadline would be in February. And the EDIC would review our proposed slate in the summer, and we would bring these to the board of governors shortly after that for full approval.

So with that, Gray, I'll turn it back to you.

CHAIRMAN NORQUIST: Okay. I think Harlan and then Barbara, I see. Oh, and Gail. Okay. Harlan?

DR. KRUMHOLZ: Thanks, Jean, and thanks for all your work on behalf of dissemination and implementation, such an important piece.

I just wanted to raise publicly that one of
the biggest challenges, I think, is to figure out how to disseminate science that -- we know that it's unusual to have such a definitive study that says, "Everybody should do X." And in addition, in a world where we want to channel forth people's preferences, values, and goals, how to place the evidence?

The Guideline Committee spent considerable time struggling with this. The reproducibility of the guidelines across organizations often isn't high, but they have methodology to do this.

Are we also thinking about the -- I know that you're going to say we need a conceptual model. But I almost think we need new ways of thinking about how a new thing, bright, shiny object, comes out. We're proud of it. We funded it. It was important.

But placing it context in the -- and how people should be using it for decision-making, especially as it just comes out, is one of the things that I struggle with because, I mean, I know in our field any given study leads to a lot of
debate about experts, and what it exactly means. And how did -- that's one of the principal impediments around bringing it to the point where the public can know what to do. And they know that there are many voices that are on either side of a particular issue.

And sometimes in a polarized way, and sometimes with conflicts of interest or particular set ideas about what right is not. A perfect example for us was the ORBITA trial, which suggested -- they did a SAM study of percutaneous coronary intervention. And the group that got the sham improved as much as the group that got the PCI. It was an elegant, beautiful study but elicited -- I mean, I don't know that the public knows quite how to interpret it because the field doesn't know how to interpret it yet, even as it's excellent evidence.

But I'm just putting that out there. One of the things, I think, in the struggle here is that -- and just because it's a public meeting -- that it often seems like, "Yeah, you get the studies. Why
aren't people following the evidence?" And it's
because science doesn't quite work like that, and
often progressive and self-correcting needs
validation. Whether something's ready for prime
time decision-making or not requires a lot of
different groups.

So I just wondered how you're thinking
about it and how we as PCORI are advancing the
thinking about how new evidence should be
incorporated.

MS. SLUTSKY: So you raised an issue that
we struggle with every single day. And looking at
the directionality of the evidence, the contextual
placement of that evidence, and actually the study
itself -- is this the largest study which has the
same direction? Is this a largish study that goes
in another direction? How long did they study these
patients? Were these outcomes the same as previous
outcomes?

So at staff level, we spend a lot of time
looking at this. There are times when we actually
convene or ask to have topic briefs of an assessment
of the literature. Oftentimes, in the applications
themselves, the PIs will describe the literature.

And sometimes in their draft final reports
and their final reports, they put their evidence
into context; not always. And depending on how the
study is actually published and that's why I
mentioned some of the -- some of the things that can
signal that this is an important study -- if there's
an editorial that the Journal has asked for, the
comments of the peer reviewers. We review those
carefully because they often give us an idea of how
important the study is.

And so some studies, probably the best
group to disseminate them to, are possibly other
researchers, so that they can think of how the next
question should be researched based on these
findings.

DR. KRUMHOLZ: Just to tag on and then let
others talk, but I just want to -- just for me, they
mean that -- the first thing is for us to fund a
group, a week consensus conference among people in -
- the experts in the field.
Not just experts, but professional sites, whoever's writing guidelines -- so that there becomes a distillation. It's not just us or the investigator, but that there's sort of a rapid ability to put this in context for the field, even putting guidelines, because then there's a second stage, which is -- once occurs, then the question is, how does it get disseminated? Do people then integrate it into practice?

But I'm just thinking. I want us to think creatively. Are there ways for us to be able to bring together folks quickly, fund it, say, "Can we make a statement about what this is? We're not" -- and not be directional? That is, we're not pushing you to say this is fantastic or not fantastic.

We're just trying to get, in a way, an early verdict on where this should go. We want to publish those impressions. And then if we are lucky enough to get a few that everyone is saying, "This is really wonderful," then putting a lot of push behind making sure everything knows about it so that they can be informed in the choices. Anyway, just
an idea.

MS. SLUTSKY: Yeah. So I think the stakeholder meeting that we held with AHRQ last week -- I think it was last week, yeah; was it last week -- was actually really informative in that area because it was around a single study that was put in context of other studies that sort of leaned in that direction in a pretty meaningful way.

And it really gave us lots of really good ideas. So I think you've brought up some issues we're struggling with every day and trying to think about how we can, and our colleagues at AHRQ can, be leaders in the field on this.

CHAIRMAN NORQUIST: So what we're going to do was Barbara was next. And I'm going to let Francis, and then we'll come back over here to Gail and go back up this way. Okay. So Barbara?

DR. McNEIL: So could you put up slide 8 again? It's the slide you rushed by because we had it in our slides. And I didn't have a chance to look at it just now.

MS. SLUTSKY: I'm not sure which one's 8.
DR. McNEIL: It's the one with the graph of what's going to be available.

MS. SLUTSKY: Oh, okay. Yeah.

DR. McNEIL: That one.

MS. SLUTSKY: Yeah. Okay. Is that the one? No.

CHAIRMAN NORQUIST: That's the studies.

Were you looking at the overview slides?

DR. McNEIL: I have board material slide 8.

CHAIRMAN NORQUIST: Go back. There was another kind of graphic.

DR. McNEIL: There was another one.

CHAIRMAN NORQUIST: There you go.

MS. SLUTSKY: Is that it?

DR. McNEIL: No. Why do I have a different slide in my index?

CHAIRMAN NORQUIST: I don't know.

DR. McNEIL: Go back, or go forward — well, it doesn't really -- the one I had for 2018 projected had 11 for as many and four for cancer.

MS. SLUTSKY: Oh, yeah, that's this slide.

CHAIRMAN NORQUIST: Yeah.
MS. SLUTSKY: Yeah.

DR. McNEIL: Oh, okay. I don't know.

Something happened to the transitions on this one.

Well, here's my question because it relates to what Harlan just said.

So within asthma there are 14 studies, and at least on the slide that I have, within the care transitions, there are four. And then when you go to 2019, there are four on uterine fibroids and --

I'm sorry, two on uterine fibroids. Two on fall prevention, and I don't know exactly where the obesity demos fits in; I guess there are two on them.

So the question is, is there going to be some kind of synthesis of the results of these 11 asthma studies? And the second question is, I didn't quite understand what the different between obesity -- between a demo and something else was.

Does the demo mean that it's a trial and that the people can put in more credence in the results? Maybe you could just walk us through what these results mean.
MS. SLUTSKY: Sure. We just wanted to give you sort of a projection of when results were coming out. But because asthma and care transitions are the first coming out, we've been working with the project officers for both of these initiatives, and there actually is a fair amount of activity to put them into context.

And some of them hold together really well. Some of them are more individual studies that are on different aspects of asthma or care transitions.

I probably would let Joe talk a little bit more about what the difference is between an obesity demonstration project and an obesity research project. But the obesity demonstration project results are actually pretty strong, and they've just been published or --

DR. SELBY: They were -- yeah. These are from PCORnet. When you see a demo, it's in PCORnet. And they were demonstrations of the capacity to do research. So they were research studies, but they were also intended to demonstrate capacity. It turns out, as Jean said, that the two obesity
demonstration projects had very impressive findings.

DR. McNEIL: So those are the ones we saw the abstracts for?

CHAIRMAN NORQUIST: Yes.

DR. McNEIL: So is that -- well, just to push my question, so is that -- we saw the abstracts last spring, I think. Right?

CHAIRMAN NORQUIST: The last meeting. At the last meeting --

DR. McNEIL: Okay. Whatever it was. So I guess what I'm asking --

CHAIRMAN NORQUIST: Just a month ago.

DR. McNEIL: Okay. Was that what it was?

CHAIRMAN NORQUIST: Yeah.

DR. McNEIL: So presumably, that's where I need to go, and with some kind of synthesis of the asthma results, if we were to take a consensus conference the way Harlan has suggested. I'm trying to push us on to get to dissemination faster --

MS. SLUTSKY: Yeah. Yeah.

DR. McNEIL: -- just because I think it's in our best interest.
MS. SLUTSKY: Right. So we still have these other mechanisms that we can use for dissemination of these early findings, including nominating them to AHRQ for dissemination and implementation; using activities that they have as well, or collaborating with them, where we each fund different parts of dissemination,

And like I said, these are really -- this graph is really to show you the trajectory of findings. I will say the obesity findings before they actually got published -- we had a meeting with specialty and primary care clinician groups, and they actually talked about the findings at that meeting. And they were quite impressed with not only the findings themselves, but how the diversity across the country and how the surgical techniques for obesity haven't caught up with the actual findings of this research.

CHAIRMAN NORQUIST: So what we're going to do is I'm going to let Francis go and then we'll come back over to Gail. So just for people on the phone, since this is Francis' first meeting, Dr.
Francis Chesley, who's the acting deputy director of AHRC and is representing Gopal Khanna today.

DR. CHESLEY: Thank you, Gray. Thank you Jean. This is exciting.

Just one quick question. We've struggled over the years with trying to guide researchers in the DNI area with a single study and implementation versus a body of work. And I wonder, how does this portfolio of PFA's unfold? How do you balance that? And will you push in one area or the other?

And then kind of a sad question. I'm thinking of the answer, but methods of DNI wouldn't be part of that?

MS. SLUTSKY: No. So actually, actually PCORI has built a methods portfolio and a communication dissemination research portfolio. I mean, we actually hope that the evaluation -- this is more like a -- I guess if I were going to make -- what is this equivalent to in the federal funding world, I would say in R24 or demonstration projects with a very strong evaluative component.

You're highlighting, as Harlan is, how we
are struggling with how to put these within the context of evidence. And part of that is working with AHRQ evidence updates, evidence mapping. Our own portfolio that Evelyn has set up on evidence mapping, the pilot was looking at our existing portfolio. But one could conceive broadening that to take in outside evidence as well. And that's a shorter trajectory than doing a very large systemic review.

But you're right. And along with you, I've struggled with this issue when most of my career on how do you put things into context without actually delaying unnecessarily the implementation, but the important process of looking at how this had been to a larger body of evidence.

CHAIRMAN NORQUIST: Gail?

MS. HUNT: Yeah. I remember from an early meeting that we had in Palo Alto that one of the issues that's come up repeatedly is how do we actually get to implementation by primary care dogs in relation to their patients and families? And that's something -- what I'm wondering is, can we do
a PCORI study on which of these implementation interventions actually works?

I understand that it's early. But it's not so much that it's this implementation, this study, this study, this study. But do we have something that looks at, overall, here are a couple of interventions that actually get down to the point of implementation so that future researchers who will be able to use something like that when they're thinking about implementation?

MS. SLUTSKY: I wish Brian Mittman was here because he'd probably grab the microphone and say, "Well, I can tell you about that body of research." So there is a fairly strong body of research about different frameworks that work in different settings for different stakeholders.

It's not an exact science, like outcomes and effectiveness research. It's the messier type of science. But there is a pretty good body of research, and we actually hope that PCORI will continue to actually contribute to that.

There's a project that's ongoing at AHRQ,
and Francis could probably talk about that, which really -- I call it the anatomy of a healthcare system project, where it looks at different components of health systems and how you can use the knowledge of how health systems are wired to implement findings faster and better.

So I don't want to put him on the spot, but there are things that are being done and have been done that can inform this.

MS. HUNT: I know. But what I'm saying is, can PCORI, for example, help the studies that are -- the people that we're going to be funding to do dissemination and implementation --

MS. SLUTSKY: I'm sorry. Yes.

MS. HUNT: -- can they help to provide them with this kind of information so that they can move forward more quickly.

MS. SLUTSKY: Yes. And one of the things that PCORI did about three years ago was actually create a toolkit and a framework for implementation, for dissemination and implementation, that is intended to do that.
But yes, the staff of our dissemination and implementation program spend a lot of time with prospective applicants, and those applicants that actually successfully have a project awarded.

DR. ZWOLAK: Jean, this is certainly very important. But I'm also struggling a tiny bit with the idea of how we put our PCORI funded studies in context. And perhaps if you could help my describing who you foresee as successful applicant vendor of this.

Will it be a scientist or group of scientists who are experts in the field? Will it be a professional society, if a group of asthma studies would be the asthma professional society, that might put this in context, or a CME vendor, for instance, at the other extreme end.

Because whoever does this, with their individual $2-1/2 million award, is going to have a significant opportunity, I think, to help put this in context. And to some extent it depends who does it. But the product comes out being --

MS. SLUTSKY: Right. So we are going to be
encouraging in the funding announcement for collaborations, the collaborations between communities, researchers, and implementers.

So I don't think the standard research model will work very well in this setting, and that's why we've created support through the engagement awards program, to help prime organizations like medical specialty societies, individual communities, components within communities to actually come together on some of these awards.

So you're right, it has to be a collaborative effective in order to get these large implementation projects off the ground. And that's how the funding announcement will be written, to encourage those collaborations of pretty diverse organizations with communities.

At the EDIC meeting tomorrow, they're going to hear about two interventions that we did in two Ohio towns, Cleveland and Columbus, where we brought all of -- they brought all the different components of the community.
They have a health collaborative in both communities, where we spent the day with them introducing them to PCORI, introducing them to some findings that we have that we know fit within the context of other findings. Enormously successful, but it really took bringing in multiple components of a community to make that successful.

CHAIRMAN NORQUIST: Okay. We'll get all that [off microphone].

DR. FERNANDEZ: Thank you, Jean. I'm very excited to see these, and I think that rigorous funding -- funding, rather, of rigorous implementation -- as you're laying out in this PFA is exactly what we need. And I'm very glad to see it.

I want to pick up on something that Gail said, which is very similar to what I was going to say. And I'm just not sure that -- I want to make sure that -- I know you know, but I want to make sure that the board, that we're all on the same page with this, which is that these are fundings for implementation projects, if I understand correctly,
as opposed to implementation science.

And I think that it is time for us to move additionally toward funding implementation science. And what implementation science can look like from a PCORI framework is pretty much exactly what Gail was saying, which is to compare different types of information approaches to see which ones result in better uptake and more successful outcome.

Up to now, there have been perhaps a few projects that could be characterized that way within the science portfolio. But in general, that has not been a focus of science, nor is it a focus, appropriately, of DNI and the EDIC because that is focused on implementing PCORI work and disseminating PCORI work.

And what I would like the board at a future meeting to think about is would not we're ready to add an implementation science component to our scientific portfolio that would allow us to tackle questions like this. So a perfect example is in anticoagulation. It's been known since the 1980s that anticoagulation prevents strokes. There are
now newer medications that may result in a higher uptake.

However, the huge gap in this is getting uptake of any medication whatsoever. What is called for is less implementation -- is implementation. But what is even more called for is implementation science. What is the best way to get uptake around this for house systems?

And I think that's where we as a board will have an opportunity, I hope, to put on our agenda to talk about that in conjunction between the SOC and the EDIC, and put larger amounts of funding, perhaps, behind these sorts of questions.

But in the meantime, I want to say how happy I am that we are doing implementation and broad dissemination. And I'm also really glad to see the panoply of options that we have around that. So I hope this was helpful. Thank you.

MS. SLUTSKY: Thank you.

CHAIRMAN NORQUIST: Thanks. Christine?

DR. GOERTZ: Yes. I just wanted to note also my strong support for this initiative. I think
it's really important. I know the devil is going to be in the details in trying to provide the appropriate amount of guidance to investigators while still leaving them the opportunity to be creative on their own. That looks to me like as you're starting to set this up, that you're doing a good job of walking that very difficult line.

On a separate but related note, Jean, I just really wanted to compliment you and your staff on the excellent job you've already done in disseminating information on the PCORI website regarding the studies that are already available.

It really is -- I don't know if the board has had a chance to go and look at the website and look at how the study findings that we already have are presented. But it's really well done. It's a model for others to follow. So thank you for the excellent work.

MS. SLUTSKY: I appreciate that. And I'm looking around the room, and there are lots of people here. But as of late Friday we had 101 studies that have research project pages with a
variety of information on them. So that's a true milestone for PCORI.

CHAIRMAN NORQUIST: Yes. Thanks to Jean and your staff and these other documents that we've been using up on the Hill and with other people have been very helpful. I think you've gotten a number of suggestions here, one about the implementation science thing. I think we can bring that back.

I think Harlan's point and the others about putting these things in a context and understanding what's really ready to be used. And then I think Barbara's big push about the quicker we can move it, the better, which is the other thing that we're hearing. Right?

Okay. So what I need now is a motion to approve the development of this PFA.

DR. FERNANDEZ: So moved.

CHAIRMAN NORQUIST: Alicia. And

CHAIRMAN NORQUIST: Okay. Then a second?

MS. SLUTSKY: Second.

CHAIRMAN NORQUIST: Gail. Okay. So I need a hand vote here. All those in favor?
[Hands raised.]

CHAIRMAN NORQUIST: And is anybody opposed?

[No response.]

CHAIRMAN NORQUIST: Okay. Anybody abstaining?

[No response.]

CHAIRMAN NORQUIST: All right. Allen, are you on the phone?

[No response.]

CHAIRMAN NORQUIST: No? Okay. All right. So thanks, Jean. Now you have something to do.

MS. SLUTSKY: Thank you.

[Laughter.]

CHAIRMAN NORQUIST: As if you didn't have something to do. Right?

MS. SLUTSKY: I have so much time on my hands, I don't know what to do with it.

CHAIRMAN NORQUIST: Okay. So we're going to move on now, and then next item on the agenda is a Methodology Committee update. So Robin, this is all yours.

MS. NEWHOUSE: Thank you. Do I need the
All right. I'm pleased on behalf of the Methodology Committee to provide an update. And before you see the Methodology Committee members. I thank each and every one of them for all they've done to help us develop these standards, ready for presentation today.

Okay. Steve, are you on the line?

[No response.]

DR. GOODMAN: Yes, I am.

MS. NEWHOUSE: Oh, great. Very good. Wonderful. Well, if you want to intersect on anything I say, Steve, please jump in.

So in addition to the Methodology Committee, a number of the PCORI staff have been very helpful in a number of ways. And I thank each and every one of them. In particular, Emily Evans and David Hickam have worked with us quite extensively, and we appreciate all of their help and support.

So just in terms of a background, the methodology standards were required as part of the
authorizing statute of PCORI. The Methodology Committee had two roles. One is to develop methodology standards that PCORI would use to fund comparative effectiveness research.

They are intended to be minimal standards for the design, conduct, and reporting of comparative effectiveness research -- not gold standards, but minimum standards. And they were to provide guidance for researchers that use research results. So they do reflect, generally, best practices.

The process for developing and adoption of methodology standards have been standard over the past couple years. Number one, we started with understanding the evidence related to the methodology standard. Those methodology standard topics were suggested, usually from the field, from public comments, from the website, or feedback we got in open presentations.

After the summary of the evidence, we generally pull together a team of experts after review of the Methodology Committee for a consensus.
And then those standards are posted for public comment. The standards we'll be presenting today were presented to you for public comment last year and were open for public comment between October and December of 2017.

The Methodology Committee then reviewed each and every public comment and revised the standard accordingly, and then deliberated once again on the standard, and then voted to approve and recommend the adoption of standard 5, or the studies of complex intervention, and one standard for the data management plan that's really being added to another standard.

So first of all is the proposed standards for studies of complex intervention. So this was an area that we had lots of feedback about the need for standards for complex interventions. Certainly it is a confusing area in the field. There are multiple studies of complex intervention that PCORI funds.

And the purpose of these studies are really to build a rigor and transparency when the proposals
first of all, in the proposals of studies that PCORI would fund, in the conduct of studies that PCORI funds, and in the reporting of those study results.

So there are five specific standards. The first is to fully describe the intervention and comparator and define their core function. So it's important in a complex intervention to be very clear with that core function to then test the fidelity of the core function, as well as understand the contextual variables and other variables that may affect these complex interventions.

A complex intervention, by nature, has multiple components that sometimes interact. And the opportunity to be very clear about the intervention and comparator will give us more confidence in the results that are generated.

Second, to specify the hypothesized causal pathways and their theoretical basis. So this standard is based on the empiric support for the intervention as well as the mapping to the intervention and the outcome.
The third is to specify how adaptations to the form of the intervention and comparator will be allowed and recorded. So the function of the intervention shouldn't be changed. But there are a number of ways that the intervention could be adapted, as you might think that a rural hospital may adapt a diabetes program or intervention a little differently than an academic health center.

So there'll be differences in how the form -- there may be some web-based support. There may be some different tools that they use. But the function stays sound.

The next is to plan and describe the process evaluation. So these complex interventions are generally tied to some kind of process, being very clear in that process what that process is, how you're going to measure the process in the comparison group. It's incredibly important.

And the last is to select patient outcomes that are informed by that causal pathway, that causal pathway that links the processes to the outcomes and any covariates that might need to be
described as well.

So those are the five standards for complex interventions. The next recommended new standard is in data integrity and rigorous analysis. I don't need to say much about how important a data management plan is to any study a priori, being very clear about where one is going to get the data, how it's going to be collected, code books, the metadata; and assuring that the data collection could be reproduced, and when we're in the analysis stage, that it's very clear what the data represents.

So this is another standard that will increase transparency and reproducible of our research results. It would be a standard that's added to the current standards on data integrity and rigorous analysis.

And this standard just describes what should be included in the study protocol. Specify a data management plan that addresses, at a minimum, the following elements: collecting data, so how is data collected; how is data organized; how is it
handled, who has access to it; describing the data, preserving the data, and sharing the data.

So these two sets of standards have been approved by the methodology committee. We're recommending that the board adopt these six methodology standards today. The next steps would be to include them with the addition -- with the standards that are already in place. And upon adoption, they'll be implemented for cycle 2 funding, which will occur in the fall of 2018.

We'll also work toward updating the methodology report, which is expected to be done in June or July of 2018.

And in addition to those activities, just to update you on our continuing work, we're still doing some development of standards in the area of data quality, individual participant data meta-analysis, and qualitative and mixed methods.

Now, the individual participant data meta-analysis and qualitative and mixed methods were two areas that we also received public comments and recommendations for additional standards. So with
that, I would say those are the two that will be coming to you next for a request for posting for public comment.

So with that, I'll stop and answer any questions that you may have, and recommend adoption of these six methodology standards.

CHAIRMAN NORQUIST: So let's start -- Alicia, I think, is the only one I see.

DR. FERNANDEZ: Thank you, I was really happy to see these, and completely agree that this is really great.

My question has to do with the data collection one and the level of detail that will be required of investigators. And without getting too much into the weeds, I'm a little bit scared of the responsible both from the merit review side and on the investigator burden side, even though I completely concur that these are reasonable standards.

Will there be actual examples in the methodology report of how to respond to these data concerns? And to what extent will they -- in your
view will they really require deep additional work on the part of investigators?

MS. NEWHOUSE: Yeah. These are just part of good clinical practices. So it's really not asking for anything other than what we should be doing if we're submitting a proposal a priori and planning our data plan.

And it's a matter of making sure that we used the approach that we designed, that we captured the data the way that has integrity, that there's transparency to what we're doing, and that the data capture is fully understood. And there's a code book, a data plan.

So it really isn't anything more than we should be doing anyway. The question about, will there be an example on the website, I'll have to ask for some help from the PCORI staff. We did post an example of a standard PCORI report, but I don't believe there's anything now.

CHAIRMAN NORQUIST: [Off microphone.]

SPEAKER: Thank you. So, Alicia, one thing to notice is this was in the study protocol, not the
study proposal or application. So it's the detail that would be in the protocol after the study is funded. I heard you say thank you were concerned about merit review.

   DR. FERNANDEZ: Then in that case, it is very much what we already do. The one thing that struck me is the data-sharing plan and whether that can -- that is sometimes not something that people have thought out in advance. And to a certain extent, we should push for people to think that out in advance. But as you know, it can be a highly complex issue.

   DR. SELBY: I'll just say to that that tomorrow at the RTC, we will be discussing a nearly fully fleshed out data-sharing policy, which is the product of both extensive public comment, received public comments, and a pilot study.

   So within the next month or two, I think a data-sharing policy will be coming to the board. And you are right that that will be -- there will be some pushback. It's anticipated that there'll be pushback there.
MS. NEWHOUSE: So Steve, I wonder if you want to jump in with any comments here.

DR. GOODMAN: No. You've pretty much covered it. I do think that even in a protocol, this can be handled very, very expeditiously. We just want to make sure that people are thinking of each of the elements and aren't saying things like, "The data will be stored in an Excel spreadsheet," et cetera, et cetera.

So these are the elements of, as Robin said, good clinical practice. But we're not sure that all our researchers are following these. So it's not meant to be onerous. It's just simply describing what they're doing, assuming that what they're doing is good practice. And if it isn't, then we have a chance to modify it.

DR. KRUMHOLZ: So I want to go back to -- thanks, Steve and thanks, Robin. This is great. And I want to congratulate the Methodology Committee for taking on a very difficult issue.

I want to go back to one of the themes that I've been raising within PCORI for our continued
consideration because of its relevance in particular -- this issue of complex interventions.

Where I've seen the most problem with the complex interventions, which are highly context-dependent, is that they are developed, thought of, by an enthusiast who's got a good idea, or who's team's got a good idea, and then implement it locally or within a small range of friends and family sites in ways that leave questions about the generalizability and reproducibility ultimately because of high level of enthusiasm.

For me, the entire study, in a way -- not even just talking about cognitive bias, but at least I've seen it. I've seen my own place. I've seen studies I've conducted myself where I wonder if the way that we've actually implemented it, there was an active ingredient.

But the active ingredient was surrounded by the best that we could optimize everything, and our enthusiasm, and so forth. And often, they're not blinded. So there are all these ways that this gets in, and you guys are addressing these.
But one if the ways that I've thought, again, for PCORI to proceed is that somebody has a great idea for a complex intervention. And then we separate the implementation of the study from the person who's come up with the idea, in that we've created an arm's length relationship where we now go out for bids for groups that want to actually try to implement this study. The person who's the originator is the architect.

But they're not necessarily a general contractor because they're basically setting out -- it's going to be their building. It's an I.M. Pei building. No one says, "Who's the one who actually built the building?" It's their design. They are going to be in charge of this.

But the actual implementation, what we're interested in, is does this thing work wherever you put ore in the places in which it's intended to work? And does it get the kind of effect that we hope to find. And I just think maybe this is just something -- and I'm not suggesting -- this looks great and is going to be an advance.
But I also just want us to be thinking about -- because this is ultimately all about the implementation science, by the way. And I 100 percent agree with Alicia about the importance of implementation science.

But the issue of implementation science ultimately becomes, "How do you move away from anecdotes of -- or what works locally to things that can actually scale, and yet be flexible enough to be refined for the constraints of a particular environment?"

And so anyway, I just think this issue of complex interventions will remain a very important topic for PCORI for -- from here on. And our struggle with this, both in what we fund, how we fund it, how we generate the knowledge. And then how we're sure that ultimately gets disseminated is something where we can break new ground with regard to how that's done.

And I just think these are particularly susceptible to the kind of contextual influences that may, in the end, undermine their
generalizability. And it's something we need to think about.

MS. NEWHOUSE: Thank you.

CHAIRMAN NORQUIST: I need a motion to adopt the --

MS. GOERTZ: So moved.

CHAIRMAN NORQUIST: Yeah, Christine.

MS. SIGAL: Second.

CHAIRMAN NORQUIST: all those in favor, raise your hand.

[Hands raised.]

CHAIRMAN NORQUIST: And anybody opposed?

[No response.]

CHAIRMAN NORQUIST: Anybody abstaining?

[No response.]

CHAIRMAN NORQUIST: Okay. It passes.

MS. NEWHOUSE: Thank you all.

CHAIRMAN NORQUIST: Thank you. Thank the Methodology Committee, yeah.

[Applause]

SPEAKER: Gray?

CHAIRMAN NORQUIST: Oh, yes.
[Off microphone discussion.]

CHAIRMAN NORQUIST: Anything before we break?

MS. NEWHOUSE: No. They were posted for comment, yes. And we incorporated all the comments into our revision, which you now have. And so they aren't posted publicly, but they will be now that you voted. Yeah.

CHAIRMAN NORQUIST: Okay. So what we're going to do is take a break until 1:00 p.m. Eastern Daylight time. And then we'll be back then.

[Whereupon, at 11:53 a.m., the meeting was recessed, to reconvene at 1:00 p.m., this same day.]
AFTERNOON SESSION

[1:01 p.m.]

CHAIRMAN NORQUIST: Okay. We're back on the telephone, so I need everybody to sit down. Harlan? Okay. So we're on live now, so we need to go ahead and start.

So welcome back to those of you who are rejoining us for the afternoon session. And I'm going to turn us over to Gail Hunt, one of the board members, who's going to introduce our next panel, which is our stakeholder panel. So Gail?

MS. HUNT: So good afternoon, everybody. Just to recap for those of you that don't remember, PCORI's mission from the beginning has really been to develop priorities for questions that should be addressed by research; to conduct the research for that; and then to look at evidence of helping patients and families, I might add, to make more informed healthcare decisions. So that's really at the crux of what we do.

And I'm sorry that Harlan Krumholz just left the room because at one of our very first
meetings, he's the one who said, "Patients are our true north." So that's what PCORI's really all about. And I think we all believe in that very much.

So we have taken that concept of patients being our true north and really infused that into the culture of PCORI. So, for example, we require that there should be patients and caregivers on our Merit Review Committees; also that they be involved in actual design and dissemination of the research that we do. So we've tried to ensure that all of the research that PCORI does is patient- and family-centered.

While we've made great strides, I think, at bringing patients to the table for this, and we can see it not only in PCORI's research but in research being done by other organizations that now have adopted this and have -- are bringing patients and families into their research design, but yet patient groups -- and add the patient advocacy organizations -- have talked about how sometimes it's very difficult to get their research funded, to
understand how they can best be employed by the research process, and how they can put their stamp, as it should be, on the research so that it's patient- and family-centered.

So with our reauthorization coming up, as all of you on the board have the top of mind, we thought it would be good to hear from a couple of key constituent organizations about patient engagement and how PCORI can do better in the future for patient and family engagement, again reaching down to help improve healthcare decision-making at really the patient, the primary care doc, and the family level. That's one of our major missions.

So with that, I'm going to introduce two of the people that we have invited here. One is Bari Talenti, who's executive vice president for advocacy at the National MS Society. And the other is Sohini Chowdhury, who's deputy CEO for the Michael J. Fox Foundation.

And then after these two ladies have spoken, we're going to throw it open and have board questions. So Bari, you want to take it away?
MS. TALENTI: Great. Thanks, Gail, and thanks for inviting us to be here today.

So I've been asked to break this down a little bit and to talk about what has worked well, what could be a little bit better, and then just some thoughts about reauthorization. So I'll talk a little bit about that, and then I'm looking forward to some interactive conversation towards the end of our presentation.

So PCORI has worked really well and really diligently to develop an understanding of multiple sclerosis. And I think that's one of the more complex things in funding a wide range of research areas, is to really develop that level of understanding. And that really can only come from hearing directly from people who are living with and affected by the particular disease or illness.

And we started at the National MS Society. We had a connection to Joe soon after PCORI came into being. And we had some initial conversations, and really started to talk about what would that look like for PCORI, to make sure that they
understood MS, and understood it from the
perspective of people living with the disease,
understand what patients are really looking for from
research.

And that's really the only way that we're
going to get to that place where research is driving
towards the answers that patients are looking for
rather than just research that's based on what
researchers and investigators are interested in from
the scientific question.

So there's a lot of that research that
happens, and not as much that happens that's really
looking specifically to answer the questions that
people living with MS or other diseases are asking.

And so PCORI has really done an excellent
job off listening to people with MS, and pulling
together a number of different sessions where there
was an opportunity to hear directly from people with
MS; to hear from clinicians who were directly
treating patients with MS; and to listen to family
members and to really hear about the impacts that MS
was having and how PCORI could weigh in and make a
difference in the research that PCORI was able to fund.

So through that, there have been a number of different areas that PCORI has looked at that are really specific to MS. And they really align with the questions that people with MS are asking the National MS Society, and what people with MS are talking about that we see through our tracking of what's coming up on social media, through surveys that we do.

So the PCORI research is really narrowing in on newest questions that people with MS are as I, asking looking at some of the top symptoms that people are having that have been really difficult to find good solutions and answers to, like fatigue and pain.

And for a long time, people with MS would say they have pain, but that was kind of dismissed by the medical community because it's not the typical pain that you find. And we don't really have good answers for how to address that type of pain.
And fatigue is really quite common among people with MS, and really has impact across living with the disease. And is probably one of the reasons that people stop working so early in the disease course.

So while there's a lot of focus on the symptoms of MS and in treating the disease itself, PCORI is really looking at some of those answers for what's going to have the biggest impact on people with MS to live their life well throughout the course of their disease.

So the symptoms like pain and fatigue, really looking at Teller [phonetic] rehabilitation, which is incredibly exciting for people, so we can find answers for people -- again, not just in the symptoms of the disease, but really looking at how do we find answers for people no matter where they live, no matter the course of the disease that they have, to be able to really engage in some of these solutions that we hope the PCORI research will uncover.

And then recently some very exciting
research, looking at what's the best pathway on
disease-modifying therapies for MS? Do we start at
early aggressive treatment and then work down if
people break through those treatments? Or do we
start at some of the more traditional maintenance
therapies and work our way up?

And again, these are questions that people
with MS have been asking. And this in particular,
with the disease-modifying therapy, is because we're
fortunate to have so many disease-modifying
treatments for MS, more than a dozen.

We're always at this place where insurance
coverage looks really different in some places, and
it's not based on the kind of data and good research
that we all want it to be. So people with MS could
have a different experience of what disease-
modifying treatment may be available simply based on
the insurance coverage that they have.

And so this research is really critical to
understanding those answers. So for people with MS,
for health insurers, and for the health system at
large, they're really getting to the health outcomes
answers that we need, both for the individual but also from a population basis, and really to have an impact on the healthcare system.

So the National MS Society funds research every year. We fund between 40- and $50 million of research every year, so a sizeable number. But we don't have the resources that PCORI does. And so the type of research that PCORI is able to fund just would not be happening otherwise.

And I think that that's -- really, one of the key things to think about as we move into reauthorization is to be able to talk about the spectrum of research that's happening, and where PCORI fits within that.

So there is a tendency on the Hill to sometimes talk about all medical research as being duplicative; if it's happening in one place and another place, it must be the same research that's happening.

And we know that's not true, and I think that that's something that's incredibly important for PCORI to be able to emphasize as we go through
those reauthorization talks and to really point out the differences about the research that's happening here, how it's different than what's happening in any other place, and how that matters both to individuals but also to the health system at large. That we hope they'll have as they're working towards. So talking a little bit about what could be better as we all continue to work together. The comparative trials that PCORI does are very expensive, and we all know that. And while PCORI is providing robust funding, we do still have, at the National MS Society, PCORI-funded researchers that are coming to the National MS Society for supplemental funding.

And so it might be worth exploring whether it's time to do less projects and more robust funding, or to really be talking with the researchers about the level of funding that they need to make sure that they're having sufficient funding to get the outcomes that we hope they'll have as they're working towards that.

One of the other things that researchers
have talked to us about is that while comparative
effectiveness studies are much needed and they're
likely only happening here, they still are more
conventional studies that are happening. And it's a
rather conventional peer-reviewed process that's
happening through PCORI.

And so there might be opportunities to
explore some more innovative approaches to
comparative effectiveness, innovative trial design,
and alternative trial design that are going to help
us get to answers for people with MS and others in a
quicker way.

We have these discussions quite a lot
within the MS space as we don't have biomarkers, and
especially as we're focused within the MS Society a
lot on progressive MS because there's only one
treatment right now for primary progressive MS.

How do we look at designing trials in a way
and finding those outcomes that get us those answers
in a quicker way? There's a lot of reliance in MS
on the EDSS Scale to measure disability. There's
also a lot of agreement that people don't love the
EDSS scale, but it's what we currently have and it's what the FDA considers.

So there might be opportunities to look at alternative ways to measure disability as a community and to maybe pilot this through some PCORI pilot grants or innovation projects or some method of funding that PCORI could develop.

So I think -- one of the other things that's been brought to my attention recently has been through the patient-powered networks. And there is one in MS, "I Conquer MS." It's been very successful, and we've worked quite a bit with the group that is behind that accelerated cure project.

And I can also share that a number of the research proposals that come to the National MS Society for funding are utilizing "I Conquer MS."

So that's great to see, to see that the "I Conquer MS" individuals, the people who are lending their data and information and participating in a patient-powered network, are seeing use of that and who are seeing some good attention to the patient-powered networks, and what we can learn from them, and some
proposals from them.

I think as those networks are shifting a little bit, and moving, I believe, towards the People-Centered Research Foundation, I think there's been some confusion around that process, and how some of those decisions are being made, and whether patients are being engaged as much as possible throughout that process.

So, then, just again to think about reauthorization in addition to really making sure that we're talking clearly about the role, and the benefit that the PCORI work brings, and how it's different than what's already out there; but to also explore through reauthorization if there's different ways for organizations like PCORI and the National MS Society or patient advocacy groups to find ways to aggregate funding at the outset of projects to really bring that forward.

So like I said, there have been a number of researchers, funded by PCORI, who have come to the MS Society for supplemental funding. Or there are ways that we can all agree on some of those projects
and areas of research up front, and think about ways
to be more creative with some of that funding that
we can all bring to the table together; to them look
at maybe funding projects in that way rather than
PCORI funding projects, and the MS Society getting
requests for supplemental funding, trying to address
that at the outset.

So I think I'll stop there, and I look
forward to some dialogue.

CHAIRMAN NORQUIST: Sohini?

MS. CHOWDHURY: Hi. Good afternoon. Thank
you so much for the invitation to join you today.

Just as a little bit of background for
those of you who may not be familiar with the
Michael J. Fox Foundation, we were funded 18 years
ago with one goal, which is to aggressively fund
research to find new therapies for patients, and in
the 18 years since we were founded over $730 million
of research.

This year we are looking to fund $86
million in research. And so, on average, we provide
between 80- and $90 million in research, focused
primarily on the translational clinical spectrum of their research paradigm.

What I was asked to do today was to provide some feedback about the interactions that we've had with PCORI. And in this situation, we've actually had two interactions, one in which we were -- we applied for funding and we were an awardee in that experience.

And then one instance, which I believe is unique in -- relatively unique DFO, is that we were awarded funding, and we actually declined that funding.

And so what I'm here to talk about today is our experiences in both of those instances, and hopefully then go into some interesting discussion with them, with my panelists and you all.

So let me start off with our first interaction with PCORI. So we applied for and received a PCORI engagement award for a project entitled, "Educating and Engaging Clinicians to Strengthen Patient Engagement in Parkinson's Disease Research."

This grant specifically provided funding to
help support clinical outreach that we conducted between 2015 and 2017, which was aimed at helping clinicians build a research partnership with their patients by increasing their awareness of and enthusiasm for Parkinson's research.

And so specific activities that PCORI funding helped us -- helped support were webinars for CME, in-person clinician events, physician-authored articles related to PD, and the development and distribution of print and online materials.

And for us, this was incredibly valuable. This funding provided resources that we would otherwise not be able to dedicate to be able to try to build that clinician network and encourage that interaction between clinicians and patients.

So it's extremely positive, and it was a game-changer for us in helping to kind of jump start our clinician outreach network. And generally, the experience through this funding with PCORI was incredibly positive.

Our program officer was thorough, very easy to reach, incredibly helpful, was proactive in
making sure that if we seemed confused about anything, was there, et cetera. So it was a great interaction with the team who was assigned to help sort of steward and administer this grant.

The templates and the process by which we would submit information or request information -- again, incredibly easy to follow, seamless, a really, really positive interaction.

The one area that we were a little concerned about and was something that ended up being a larger concern in the second interaction we had with PCORI was more related to the administration and reimbursement process, and the amount of time it took for our staff member, who was a PI of this particular grant, to actually liase with our finance team to be able to get the information to submit on a monthly basis the invoicing for our grant payments.

And this was just something that we -- we fund research. So we had a particular way in mind of how we thought it would go. And I think what surprised us in this interaction was just how much
time it took both our finance individual, the member of our finance team who was assigned to this project, as well as the PI of this project, to sort these things out.

And that could have also been impacted by the fact that we were operating in a period of turnover. And so there wasn't necessarily one assigned person in the finance team. Instead, we were emailing and a general account, et cetera. But it was something that just flagged it for us because we did have issues in that particular area.

But by and large, it was again an incredibly positive experience and a game-changer in that it provided funding for us to move into a direction that we otherwise would not be able to. And it was with that really positive experience that we saw there was a request for funding for the PPRN phase 2 program. And so we decided that we were going to apply for that funding. And this was a much larger funding bucket than our clinician research project.

And the project that we requested funding
for was a study called Fox Insight. And so I'm
going to take a moment of your time to just provide
a little bit of background on Fox Insight because
it's actually quite pertinent to why we ended up
declining the over the million dollars that we were
awarded.

So Fox Insight is an online longitudinal
study that is designed to source data directly from
patients and control through webinars -- excuse me,
through surveys, online surveys, et cetera. At the
time of funding or at the time of us submitting our
proposal for funding, Fox Insight was already built.

It was in beta mode, and we had over 2500
participants that were participating in virtual
quarterly visits. And we had a subset of
participants who are also providing objective data
through the use of wearable technology,

So we requesting funding, $1.2 million over
three years, to specifically move from our beta mode
of operations to an official launch, with the goal
of enrolling up to 100,000 Parkinson's patients --
that's about 10 percent of the estimated U.S. PD
population -- 100,000 U.S. Parkinson's patients and 25,000 controls over a three-year time span. We were also anticipating using the funding to help us build the database for this study. We were collecting the data, but at that point in time, we had the goal of making the data available. We had experience with this from another project. So we want to have a real-time open source data portal available for researchers to utilize. And so the funding would help us develop that research portal, do the data curation, et cetera, to make the data available.

And lastly, to integrate the Fox Insight study with another online tool that we had developed called Fox Trial Finder, which is what I like to call a Match.com that connects volunteers to trial teams that are looking for them. And so the idea here was if you were providing information about your disease experience on a quarterly basis, and you're able to connect that with Fox Trial Finder, you would be getting matches that would be based on the real-time sense
of where you are with your disease and your symptoms. And trial teams will be able to utilize that information to better match and reach out to patients who may be a good fit for the studies that they were running.

So we submitted the application, and we were really excited to hear that we were going to be approved for funding. And in setting up this application, we, I think mentioned, requested 1.2 million in funding over three years.

The funding was -- the PCORI funding was going to support about 45 percent of the time of our primary PI, who is a staff member in MJFF, who was overseeing Fox Insight, and a very, very small percentage of the time of all of our multiple vendors that were basically running the technology and who would be tasked with building the new capabilities and maintaining ongoing capabilities as we did this buildup.

Funding was also requested to convene meetings with a researcher and patient advisory task force, and also for site grants, to support minority
recruitment into the study.

On our end, the Fox Foundation was planning -- we did not include this in a funding request to PCORI -- but we were, in parallel, going to cover the costs associated with all other key personnel in the study, including five staff members and two consultants. And all of this funding would be provided through MJFF donor funds. We were also going to be covered any supply costs that were needed for the study through our donor funds.

So PCORI was incredibly generous with their time during the application process. They were incredibly helpful in answering questions, et cetera. And I have to say they were incredibly gracious as well because we sort of threw them a curve ball in the middle of this, where after we submitted our original application, we reached back out and we said, "Hey, we have good news and bad news. The good news is that we have made a lot of progress in bringing on board a new collaborator to Fox Insight."

23andMe had agreed to become a co-PI to the
study and to provide the ability to SOC genetic data
in addition to the phenotypic data that we were
collecting through online surveys. So this is
fantastic.

The bad news is that, uh, can we rewrite
our application to bring on board and represent this
new collaborator? And PCORI was just really
generous, and kind of didn't -- maybe took a deep
breath but did not blink, basically, and sort of
said, "Sure. This sounds like an exciting new
addition to the project, definitely. Resubmit,
please. Address the following, et cetera." And so
we resubmitted, and as I mentioned, we got funded
and we were extremely excited.

So I mentioned before that this is the
project where we ended up declining the funding.
And so this really started with the first step of
having the -- working with the program officer
assigned with us, who was going to take us through
the contracting and the administrative aspects
related to this grant.

And as he to know us through it, we began
to -- concerns began to be raised in that this may not be as straightforward as we thought, given the experience we had with our previous instance of PCORI funding.

And concerns fell really -- were bucketed really in three areas. The first were the requirements to comply with administrative oversight of the grant. The second was the time expected by PCORI of MJFF staff to participate in calls and in-person manages.

And the third was the recognition that this study is not being funded wholly PCORI. It's only being funded by a small percentage. The rest was coming from MJFF funding. Yet how do we balance that with the overwhelming weight of decision-making that was coming with the PCORI funds?

And so let me dive a little bit deeper into three of these buckets to explain where our concerns -- what was concerning about these three particular areas.

So in terms of administrative oversight, so I had mentioned earlier that the previous grant was
a great experience. We did notice, however, that our PI was on the phone a lot with the PCORI grant manager. And there were a lot of check-ins, there were a lot of report submissions, et cetera, and that we were having a lot of time spent on particularly the financial reconciliation of things.

When we began to see what the administrative oversight was of this particular grant, we recognized really early on that our PI, the main person running this study, could not do that in addition to actually running the study. She was incapable of it. It was just not possible.

And it's not because she did not have great bandwidth. Fox Insight was just one thing. She also managed Fox Trial Finder and oversaw our clinical recruitment activities. The reality was it just wasn't feasible for any one person who had a percent effort on Fox Insight.

And so we had to get really creative about how we could potentially manage the time and the administrative and the reporting, et cetera. And when we calculated it, we realized that across the
teams, it was -- if we thought about who would have
to be involved, it was about $150,000 a year of
staff time, or a little bit over one FTE, just
required to comply with the administrative
oversight.

And considering that we were being provided
$480,000 a year in funding through this particular
great, it was beginning not to make sense
financially to receive this grant.

So the second issue was related to time
expectation. We received news of the funding
approval in August, and as we were on boarded, we
received a meeting schedule that outlined
expectations of in-person attendance for meetings
between September and December, so a four-month time
span.

And the expectation was that the co-PI, our
CEO, and our PI, our staff member, our project
manager, were expected to participate in these
meetings. These were five meetings over four months
that comprised nine days out of the office.

From our perspective, we just could not
justify that amount of time spent out of the office for, again, one project out of many in our portfolio and where our staff were only spending a percentage of time on that particular project. It just wasn't sustainable for us. It was really about the opportunity cost of this project under requirements versus what it was going to do to our other projects in our portfolio.

The last bucket has to deal with the discrepancy between the funding and then the decision-making of Fox Insight as a study. And earlier I provided a little bit of detail about PCORI funding versus MJFF funding.

So basically, PCORI funding was providing less than half of what we needed to run Fox Insight from an annual perspective. And that included not just the direct study aspects, but it also included all of the tangential but incredibly important things related to marketing and communications for recruitment, related to the administrative bits, related to technology aspects, et cetera, statistics -- everything related. Not any of that was really
being covered by PCORI funding.

And PCORI had a lot of processes or a lot of governance in terms of how things had to be approved before you could move ahead. And while we didn't, in principle, have problems with the criteria that were being applied to the project, that's part of why we applied, because there was great insight and knowledge to be gained from an organization that was focused on patient-centered research.

The reality is, much of this project was being funded by external donors. And our donors had an anticipation that we were going to move as quickly as possible. And when we overlaid our plan versus when and how you had to provide information, get it reviewed, get it approved, get the okay to move ahead, it didn't jibe with our timeline.

And so we realized very quickly that it was not going to allow us to move ahead on the time frame that we were expecting. And with 23andMe coming on as the new collaborator, we also had added pressure to be able to integrate that very quickly.
as another partner, who is providing me sources, to integrate that quickly to move ahead. And that didn't look like we were going to be able to balance that. So that was a third area that raised concerns.

I will flag here that we were very transparent about these concerns with PCORI staff and leadership. And they consider incredibly understanding. They provided contact information of awardees so that we could hear firsthand the experiences of other awardees to understand whether our concerns were legitimate or not. They were really great at having multiple conversations at all levels of the organization to try to provide clarity and to try to problem-solve around some of the areas that we were flagging.

So I do want to sort of state here that while maybe the end result was disappointing for both of us, the entire process was an incredibly collaborative and very positive experience in that everybody was trying to problem-solve here and find the solution.
And I think that was, again, something that just reinforced to us that there was great value in trying to figure out how we could really take the time to figure out how we could potentially move forward.

But at the end of the day, we just couldn't make it work, and so we ended up declining funding. And I think that our decision to decline funding is really based on the uniqueness of the fact that it was already built. It wasn't being built. It wasn't an idea. It was built and we had funds already for it.

And we as an organization could actually -- it wouldn't be great to leverage other funding and get that added knowledge into it. But if we had to, we could also still fund it on our own. And so I think we are unique in that, when I think about the other organizations that we spoke at this, when we went through this due diligence process to understand the challenges that we were identifying. And so I think that's something to bear in mind.

And you may ask, "Well, if your study was
already launched and you could fund this on your own, then why did you actually apply?" And I think that it's really important to understand why we applied.

First of all, like any organization, we want to be able to leverage other dollars out there because it means that our colors could then be applied elsewhere. And we felt that Fox Insight was a great fit in the mandate, in the culture, in the philosophy of what PCORI was doing.

Secondly and perhaps more importantly, we believed it would be amazing to make sure that Fox Insight was part of that homework, to be able to provide the insight and the experiences we were having in building this online study, with the experiences and insight that other groups, awardees of this, were going through as they were building their networks and their studies, et cetera.

There is nothing greater as a nonprofit when you have limited resources than to be able to gain that real-world, real-time knowledge as you're doing it, and be able to avoid the redundancies,
mistakes, or apply the lessons learned that others have done.

And that was incredibly valuable for us because we were doing something in the Parkinson's arena that no one had done before, and other groups were doing it in other disease indications that were in some cases more advanced than ours; but in other cases, we might be able to share our experiences with them and help them avoid some of the pitfalls as we built this technology in this study.

So that was really the critical aspect of why we were seeking PCORI funding. And finally, there is also validation. People talked about getting there MJFF seal of approval, if you get MJFF funding.

Well, it works also for the foundation. There is real value add for us to be able to say, "Hey, we are a patient-focused organization, and this study is about sourcing data directly from patients. And look, we were able to get PCORI funding." And that is also really valuable. Again, it speaks to the brand and the meeting that
underpins what PCORI has built over all these years. And so while we had positive experiences in terms of the funding we received, and in one case we were not able to move ahead with funding, by and large I think what I would underscore here is that yes, there is improvement in the process of how perhaps grants are administered and issued.

But the essentials of what PCORI's doing, the philosophy in the staff in how they approach teams, has been unbelievably positive in all interactions. And so from our standpoint, there's incredible value to still try to figure out how we could potentially work with PCORI going forward.

Thank you.

CHAIRMAN NORQUIST: So Gail, I'm going to - Gail, I'll let you run the discussion.

MS. HUNT: Yeah. I was going to do that. I wanted to take the prerogative of the moderator here and ask Bari, you mentioned the fact that you thought, going forward, we ought to think about better innovative project design, that rather than perhaps doing things the way that PCORI had funded
the projects in the past, we ought to have more innovation.

Could you talk a little bit more about what you meant by that?

MS. TALENTI: So let's add to the fact that I have the JD after my name, not a PhD or an MD. So take that with a grain of salt.

But, I mean, we're looking in --

[Laughter.]

MS. TALENTI: That depends who you ask.

But I'm happy to be among my friends here.

CHAIRMAN NORQUIST: With salt. With salt.

MS. TALENTI: So we're looking at lot in the MSBs around innovative trial design and alternative trial design. And part of that is what people with MS are telling us, and part of that is what came out through a lot of the PCORI conversation.

So, because we're footnote and I'm asked, I think, to have a number of disease-modifying medications, we're almost onto that next wave of questions that people with MS have.
So some of that can be, okay, so which disease-modifying medication is going to have any impact on my cognition? What's going to protect my grain matter and brain volume? That's a big part of the next wave of conversations around MS. Are any of these medications going to help with my fatigue?

So those are some examples of adding different questions onto trials that we don't yet have the answers to; but also look at, are there shorter ways to do a trial that we can get to some of those answers?

And I think, for a lot of it -- some of it around that testimony link, and I don't think we have the answer as to how to get there. But an organization like PCORI could run pilots and help figure out, for the entire community, about how to shorten that timeframe.

What are different ways of looking at things? How do we look at those comparisons of treatment differently? And the comparative trials are going to be a little different than the traditional trials at the FDA is looking at.
So I think there's a little bit more leeway there to experiment and innovate, to try and find the shortest time frame to get to the answers that people living with these diseases are really looking for.

MS. HUNT: Yeah. So I'm going to throw it open to other board members. And Ellen, you're up first.

MS. SIGAL: Well, first of all, I want to thank both you. Extraordinary work and great presentations, and much to be very proud of.

So Bari, one of the things that specifically, I wanted to ask you is at Friends, we work on regulatory issues in terms of clinical trial designs. And we've been leaders in this field, and often are very frustrated both with the NIH and with the FDA, although this has been changing pretty rapidly.

But there are new initiatives, and I know there's a lot in cancer, so I really don't know what there really is in MS, but patient-centered trial design and innovation in trials and patient-centered
trials.

   Have you been working with them on some of these issues? Because it's very important. As you know, the metrics begin to be completely measure.

   MS. TALENTI: Yes. And thank you for that. We are working with the FDA on those issues. We were instrumental weighing in on a lot of pieces of the 21st Century Cures Act and are following those through and weighing in on the regulatory opportunities and talking with the agency.

   We've seen more innovation and more willingness to innovative in cancer, probably for a lot of reasons than in MS -- some of it is probably terminal versus a lifelong illness, so you have that. Some of it, I think, is just the disease course itself or the standards that have come to be within some of the trial designs that we see.

   We are very much interested in working with the agency on some of those alternatives. And the MS Society was involved with some initiatives called Mosaic, and I'm never going to remember what it stands for, but it's around different outcomes for
trials. And a package has been submitted to the FDA to consider some other things that look beyond just the EDSS scale that I mentioned.

So that's one example of we're trying to get some of the science to match up with what people are interested in and what we've learned about the disease over time, so that EDSS is looking specifically, really, at physical disability.

And what we know from people with MS and what we know from, now, more experience with the disease is that while people certainly encounter physical disability as a part of the disease progression, they're also encountering cognitive challenges and cognitive disability. And that's currently not measured anywhere in a traditional clinical trial. So that's one example.

And one of the pieces that has been submitted or will be submitted soon to the FDA is looking at a standard for measuring cognitive disability. But that's just one example of how we've learned about the disease over time. People are also asking different questions about the
disease. And we need to change up in the scientific and each community to that.

MS. SIGAL: I just will say Janet Woodcock is extremely interested in it. And in cancer, we have really experts. I don't know what exists in CDER on these issues. But it is really important, and I know they're moving quickly on it.

And I just have one more brief question, and I don't want to dominate. One of the issues that frustrates me with this entire field is the bureaucracy, whether it's at NIH or even at the FDA. And even sometimes we're trying not to be, but we've created our own.

The ability to really move past that towards outcomes that really matter are really important, and we need to really look at these things very carefully. So I'm saddened by the story, but I think that we at PCORI have to look at our prostheses and how to change them and to make them a little bit more flexible, depending on the disease situation and the groups we're working with.

So I hope this is a good learning
experience for us. But thanks for your work.

MS. HUNT: Mike?

DR. LAUER: Thanks, Gail. So I'm Mike Lauer. I'm one of the deputies at records at NIH. This is a great story, so thank you for sharing the story with us. And I want to thank PCORI leadership for giving us the opportunity to hear this story.

So we get it from both ends. On one end we're told that our grant oversight is way too lax, and whenever something bad happens, which invariably it will, it's because we were asleep at the wheel. So that's one side. And then on the other side, we certainly have heard stories like yours before, that we're way too unsure, said that we're taking up way too much time, that there's a lot of unnecessary administrivia. So help us through this a little bit further. I'm echoing what Gail just said.

MS. CHOWDHURY: Yeah. It's a great question. And of course I think there's recognition that PCORI funding is coming from taxpayers, so there has to be more stringent oversight, perhaps, than our -- or perhaps I shouldn't say "stringent."
That's the wrong word.

The needs of oversight, perhaps, are different than it may be for a private foundation or whatever it may be. I think what I would say is that if I look back on that, and I was looking at my notes and all the email correspondence and everything that happened August 2015 as I went through this -- and the CEO and I are actually the only people left at the organization who lived through this.

And so it was an interesting time to go back at that. And I think my takeaway is flexibility in understanding where a project is that is being funded by PCORI.

And again, I think this is what I would underscore, is that when we spoke with the groups that PCORI staff put us in contact with, and when we looked and heard about the other projects that were being funded through the PPRN, most of them were in very, very early stages. And the funding from PCORI truly was funding to make that project happen.

And I think that the oversight of that
entire program was built under the assumption that PCORI funding was going to be the seed funding to generate that. And as a result, the level of oversight in when key decisions would happen, how they would happen, who had to feed into it, et cetera, were structured in that manner.

I would say that the answer is not necessarily taking away oversight. It's about applying flexibility as to the stage of project and when it receives funding. A study that already exists, that have people enrolled, that have an IRB that people consented, where data are being collected, is extremely different in terms of the decisions you can apply or how you apply it on an ongoing study versus a study that hasn't even been formulated.

So I think that that lack of flexibility in terms of thinking about a project or a study that is over here, with consented individuals already providing data, versus something that just has a project design or a protocol synopsis, and not see in that, that's probably to focus on and to think
about, how do you change or how do you adjust the way that you solicit information from your awardees, and where you get involved and the time frame for that, probably needs to be different on both sides of the spectrum.

And that's how I would tackle the issue, as opposed to a general statement saying, "There should be less oversight." Because the oversight's important.

MS. HUNT: Larry?

MR. BECKER: Thank you very much. Those Were terrific presentations.

So as you know, we have literally hundreds of projects, and I'm going to take on MS. Okay?? So we have projects in MS. And my real question is: Since the MS patients are your audience, and we're going to have results from the various projects.

What's your process to help us to disseminate and ultimately implement the results from these research studies?

MS. TALENTI: That's an exciting think to think about. And we've done some things before.
We've done sine heart blog posts before between PCORI and the National MS Society. So that's one avenue for getting information out.

But I think as a patient advocacy organization that's very familiar and works in the research space, we numerous communication vehicles that would help to provide that sort of thing. So we have quarterly newsletters and magazines. We have a website that gets about 700,000 hits a year. Is that right? A year.

We have MS Navigator system, which is people who reach out to the MS Society for information, services, referrals, case management if needed, that got about 10,000 calls or web chats, web requests, in in the last quarter. So we're reaching a lot of people with MS that provide that way to get that information out to them.

I think that there's a few things to think about with the types of information and the types of research that PCORI is doing. And one is about getting the information back to the patient, to the people with MS. And we're certainly poised to weigh
in on that.

But I think the other piece of it is more tied to the population health side of it. And how do we take the information from the PCORI-funded research and apply it to the health system and better health outcomes for people with MS because certainly what we see is that we have a big focus on shared decision-making now in our health system.

And I was telling Joe I was at the American Academy of Neurology meetings all last week, and there were lot of conversations around shared decision-making. And what I keep saying back is, we want people with MS and their healthcare provider to have those conversations together and to talk through what the possibilities in their care are.

But what I don't want to see happen is they reach a decision together. The person with MS feels really good about that. And then they find out from their health insurance that they can't go down that avenue for some reason.

And so that's why I think we need to think about: How do we take the information that we learn
from the PCORI-funded projects and both get them out
to the people living with the situation, but also it
informs the health system and the decisions that are
being made there. And that's work that we're start
as well.

   MS. HUNT: Barbara?

   DR. McNEIL: Thanks. Fabulous presentations. I learned a lot from both of them.

   I have one question, I guess, for Joe and
maybe the staff. You raised the issue, and I think
that Ellen raised it as well -- or Gail did, rather,
the post chills for different kinds of experimental
designs with regard to and including -- or basing
your results on short-term -- up comes like fatigue.

   And I'm wondering -- we've talked about
this a lot, Joe. And we know that from the cancer
community there have been a lot of studies that have
used good outcomes that have a way to not come to
pass. Some have and some haven't. And this has
happened in a number of other disease states,
cardiology and cancer for sure. Sometimes they work
and sometimes they don't.
I'm wondering if this isn't the time for PCORI to solicit a review or a nice comprehensive study or short-term outcomes. And maybe they're fine, but it worries me sometimes if you have a good short-term outcome on something or other that is diametrically opposed to a long-term outcome, that's not good.

So this is just a suggestion that you might think about contracting with somebody to do a very thorough analysis across publications, multiple disease -- multiple disease states. And Ellen would clearly know where all the cancer data are.

So that was relating to your first point. And the second point relates to Sohini's point about the overhead. And I guess I was taken aback by -- I can't remember whether it was seven meetings or nine meetings by two people in a period of five motions.

So is that common, Joe? And is there something that you can do as a result of this experience to stimulation that kind of overhead?

SPEAKER: "Overhead" with money.

DR. SELBY: Yeah.
[Laughter.]

MS. HUNT: It's overhead on her end and oversight on their end.

DR. SELBY: I think the meetings Sohini was talking about were meetings -- PCORnet meetings. So this was -- the notion was that we were looking for networks to join PCORnet. And as Sohini said, she had a project that was well along that didn't have anything to do with PCORnet, and we want trying -- we wanted to shoehorn it into PCORnet because we wanted Michael J. Fox Foundation there and Parkinson's represented.

But, I mean, that was one of the main things people did in building a network is get on the phone and talk with each other. And she had a whole list of things that their project had to do back home, and there wasn't room for both.

So if that makes sense you, Barbara, we were bent mostly on building the network. And it did take some meetings.

MS. CHOWDHURY: No, hold on. I'm sorry. I missed a beat there. So this would -- the reason
MS. CHOWDHURY: No. They were two. It was the core net as well as the onboarding of the boardees into this structure. And so it was five meetings that comprised nine days over four months. And I think that that was our other thing that was very hard, is that the value of being part of this was being part of the network.

But we could not justify the time where we were based on doing that. It didn't work. Somehow we could not figure out a way to make this work very well. The onboarding in and of itself, I would say, also was extensive. It was two days. It was full-time.

So, I mean, it was just, in general, the entire kind of thing. When you looked at it as an awardee. As one aggregate level of expectation of engagement, we just could not justify it.

MS. HUNT: Yeah?

DR. FERNANDEZ: Thank you both. That was really fantastic presentations. And I've listened really carefully, and hope that we can continue to
talk about these things, and specifically, talk about the administrative opportunities and burdens for awardees, and also to talk a little bit more about short-term outcomes, though that is really a hard nut to crack, and in a certain way be better served under a foundation than under the type of scenario that PCORI does.

But all I'm saying is that it's difficult, but it's hugely important. And I think you're very aware of how difficult it is. I say this because I really have been listening carefully, and look forward to taking what you're saying to further discussions within PCORI.

So perhaps it's okay if I ask the following question of you two, which give us is: What advice would you give us on how to engage your organizations and organizations like yours in the PCORI reauthorization process?

MS. TALENTI: I think we've been having some conversations with PCORI staff for some time, and I think we would welcome further conversations about that. I think we believe that a spectrum of
medical and health outcomes research is needed to find solutions for people, and that we clearly see that PCORI has a role within that spectrum. So we would support efforts towards for authorization, and we would look at how that fits within our advocacy work across the spectrum of medical research.

But currently, the National MS Society advocates for funding for NIH research program through the congressionally directed Medical Research program, funding for a surveillance system for neurological disease conditions.

We've advocated previously for the Agency for Healthcare Research and Quality, which probably most closely aligns with some of work that PCORI does. So I think we clearly see how the PCORI work fits within the spectrum, and would welcome further conversations about that and how we could be helpful.

MS. CHOWDHURY: So the Michael J. Fox Foundation just added public policy to its portfolio about a year and a half ago. And so I would
certainly say that some learned to -- the MS Society, we are strong advocates for funding, for increased funding. And I think in this particular situation, I had discussed it over lunch.

I think, if you take aside all of the funding and the support of projects that PCORI has given all these years, and you just talk about the impact that PCORI has had in making patient centricity in research, patient engagement, a cornerstone now; and when we talk about medical research, that in and of itself is huge.

I think that we now no longer -- it is no longer -- people don't look askance when we talk about patient engagement at the same time as talking about drug development. And that is partly due -- in fact, it's, I think, due a great deal in fact, to PCORI and to the efforts of normalizing this concept of patient centricity in drug development and medical research.

And so, from our perspective, I think the work that PCORI does is invaluable. I think we, too, would welcome discussions as it becomes closer
the time frame to understand what PCORI is doing for reauthorization, and to understand what sorts of assistance or information we can provide with that process.

MS. HUNT: Well, thank you very much, ladies. This was -- oh, I'm sorry. He must have just --

CHAIRMAN NORQUIST: Right. Russell. We'll let Russell have the last -- no, she's already --

Barbara's already --

MS. HUNT: Barbara's already spoken. So go ahead. I didn't see you, Russell. You must have just cropped up recently.

DR. HOWERTON: Bari, one question. You had mentioned that PCORI was much more receptive to patient feedback in study design than some other funders you've worked with? Does your organization or you yourself carry any walking around specifically as to changes to investigatory protocol that came about as a result of that previous input? I think that would be very useful to us as a group, if we could cite very specific examples.
MS. TALENTI: I think the specific examples I could share now would be that the attention to really answering the question is that people with MS, people living with the disease, are asking. And while that's not specifically about a trial design, I think it was an anomaly when PCORI started doing its work. So a lot if the work that we would see in MS was very focused on disease-modifying treatments, a focus on more of what is sometimes referred to as the hard science.

And the questions that we were hearing over and over from people with MS were: Which disease-modifying treatment do I start on? How am I going to manage my fatigue? What can I do about pain? And those were the types of things that PCORI has been more than willing to listen and understand the actual experiences living with a lifelong chronic disease, and to find new types of answers.

DR. HOWERTON: Thank you.

MS. HUNT: So anybody else?

[No response.]

MS. HUNT: Well, thank you. These were
wonderful presentations., really

CHAIRMAN NORQUIST: Thanks, Gail, for doing
the panel, and thanks to our presenters, too.

[Applause.]

CHAIRMAN NORQUIST: So the next item on the
agenda, the Cycle 2 slate from the -- what is it,
the Pragmatic Trials, I think? So I think Christine
Goertz is our selection committee children, and
Evelyn, are you --

Okay. So thanks -- where's Bob?

DR. GOERTZ: I'll let Evelyn come up and
get set up. We actually have three slates that
Evelyn is going to be presenting today.

CHAIRMAN NORQUIST: Yeah. I just need to
go on by each one because some people are recused
from different ones.

DR. GOERTZ: Right. No, I understand.

CHAIRMAN NORQUIST: So on the first one,
Larry Becker, Michael Lauer, and Bob Zwolak are
recused from the pragmatic clinical study slate.

Okay.

DR. GOERTZ: Great. Thank you. So with
our pragmatic clinical trials slate this round, as you'll see when Evelyn starts presenting, we got pretty darn close to the targeted budget amount for these particular grants for the proposed award.

That did not -- that's not necessarily true for the other two slates that you'll be looking at today. That may be a conversation that we want to have when Evelyn is done with these three presentations.

I'll turn it over to Evelyn, then. Thank you.

DR. WHITLOCK: Thank you -- can you hear me? Oh, okay. Thank you, Christine.

So I'm going to -- just for this pragmatic clinical studies slate, I'm going to read to you the merit review criteria. And then we will -- they will be the same for all of the slates.

So just to remind you, our programmatic clinical studies, and all of our merit review, looks at six criteria carefully through the merit review process.

The first is the potential for the study to
1 fill critical gaps in the evidence.
2 The second is the potential for the study
3 findings to be adopted into clinical practice, and
4 to improve care delivery.
5 The third is the scientific merit
6 considering research design, analysis, and the
7 outcomes to be measured.
8 The fourth is the investigators and the
9 environment.
10 The fifth is that patients entered in this.
11 And the sixth is the patient and
12 stakeholder engagement in the application.
13 For Cycle 2 of 2017, the pragmatic clinical
14 studies announcement received 54 letters of intent.
15 We invited about half of these to submit full
16 applications, and we received about two-thirds of
17 the applications invited.
18 So we got 16 full applications. Out of
19 that, we are bringing to you today five
20 applications, which is a funding rate of about 31
21 percent. So this is a really good funding rate for
22 recent experience, and we're very pleased about
that.

I'm going to give you the overview of the five projects together. And then I will talk through each of these in a little bit of detail so that you understand them better. And just to remind you, these have all been through merit review. They've all been through methodology consults. They've all been through discussion at the selection committee. And these are all recommended for funding for the full board by the selection committee.

The first project, which is bolded, is bolded because it is a resubmission. And it is looking at family-centered approaches to childhood obesity treatment, a very important issue for families and for children.

The second is comparing two different medication approaches for a rare disease, pulmonary mycobacterium ABM complex disease.

The third is looking at individuals with serious mental illness, and various ways of supporting them when they also have medical
comorbidities as well.

The next one is to look at very pragmatic and efficient ways of improving access to tobacco cessation services at the statewide level for underserved patients in federally qualified health centers.

And finally, we have a comparison, a head-to-head comparison, of two formats for evidence-based treatments using cognitive behavioral therapy for children and adolescents with anxiety.

The first project, as I mentioned, is a resubmission. It's a $13.9 million study looking at the comparative effectiveness of two recommended approaches to the treatment of obesity in children.

The first is an initially intensive family-centered approach to addressing obesity, and the second is a more staged approach. And the study will be looking at the impact on weight among children, and also the weight of the parents, in underserved families in a primary care setting. Children ages 6 to 15 and their parents are eligible, and as I mentioned, there's a emphasis on
low-income families.

I mentioned already what the two interventions are. And the primary outcome will be focused on the reduction in weight of both the child and the parent. But there are important secondary outcomes such as quality of life, mood, coping with bullying, and cardiometabolic outcomes because we often see that these children experience premature elevation in blood pressure, in their lipid levels, and even problems with glucose tolerance.

This is a two-armed randomized, controlled trial. It's a large sample size, 1296 child and parent dyads divided between the two arms. The active intervention will be 12 months, and we will be following these children and their families over an 18-month period.

This is an important study to deal with this problem that continues to grow in the United States. It will allow patients, primary care providers, and health systems to understand what is the most effective and efficient way to approach obesity treatment for children and their families.
It may also help clinicians and payers understand the different resources requirements related to these different approaches. Obviously, it is targeting a population that is much affected by the condition of obesity, but often is under-accessed in terms of treatments. So low-income and minority children are the focus. And the importance of the outcomes, particularly the secondary outcomes but also the primary outcomes, have been endorsed by those that will be affected by the research.

There are advisory panels mentioned here that will be involved across the study and will be important for the dissemination of findings. As you know, there are guidelines around how to help clinicians and families and young people deal with this condition, so this information will be very applicable to practice.

The second study is looking at two different approaches to multi-drug treatment for pulmonary mycobacterium ABM complex disease. As I mentioned, this is a rare disease, but an important
disease. It will look at adults that are culture-positive for this type of disease, but that have not developed cavitation in their lungs, or areas of infection in their lungs shown by a cavity. And they cannot have been treated in a prior way, so that we get people who are new to treatment.

We will be comparing -- or, I'm sorry, the study will be comparing two different antibiotic regimens, one a two-drug antibiotic regimen, listed here; the second is a three-drug antibiotic regimen, which is currently often what is the treatment of choice. So what people are interested in is whether the two-drug regimen, which may be more easily tolerated, will be as effective or non-inferior to the three-drug regimen.

The primary outcome therefore will look at what is a culture of material from the lungs as 12 months, and is that -- does that show no evidence of the infectious agent? And we will also be looking at the tolerability of therapy. Secondary outcomes are listed here, including health-related quality of life, adverse event rates, and development of
antibiotic resistance.

This will be a multi-site, randomized, controlled trial. It is necessary, because it is a rare disease, that it's recruiting a robust sample to be able to answer this question. The duration of the treatment is 12 months, and patients will be followed up for at least 12 months. And the cost is $6.2 million.

This is thought to be capable of providing the most definitive evidence that could be available for informing the evidence-based treatment of this disease. And as I said, because it's expected that the two-drug regimen will be better tolerated, this evidence could be very helpful for people in being able to both adhere to the long-term treatment that's necessary and that would be also effective.

And this actually came out -- this particular question came out -- of a PCORI engagement award. So it shows the input of the engagement award process into research project development. There's a patient advisory panel and other study advisory panels of those that will be
affected by the research. And there are partnerships in place for the dissemination of the results.

The third project addresses a seriously burdened population, those with chronic mental illness or serious mental illness who experience, on average, a 25-year decrement in life expectancy. And this will look at, among adults age 18 and older with a serious mental illness diagnosis and one other poorly controlled medical condition, what is the comparative effectiveness of two different group approaches to helping these individuals manage their own health more effectively?

So this will compare the effectiveness of the integrated illness management recovery program with a well-established chronic disease self-management program. These two programs are equivalent in the amount of intensity of the interventions, but are different in that they are led by different types of clinicians or, in the case of the chronic disease self-management, with some tier support.
They also have different types of intervention. The integrated illness management recovery is 16 weeks of one-hour sessions with two up-front boosters, whereas the chronic disease self-management is over six-week program with longer duration. So they're different in content. They're different in how they are led. And they're different in the way that they are packaged.

The outcomes will be looking at the impact primarily on the ability of these individuals to manage both their physical and mental illnesses, as well as a measure called patient activation, which correlates with self-change and health behavior.

Secondarily, this study will look at physical and emotional health, and will look at surrogates of wellness, which relate to the use of the emergency department as well as hospitalization. This is a randomized, controlled trial, although it will employ mixed methods as well to get at some of the experiences that the individuals will have.

The sample size is 600, the length of follow up is 12 months, and it's a little -- about a
$7.5 million study.

As I mentioned, because of the known decrement in life expectancy suffered by these individuals, ways to engage them in managing their physical health as well as their mental health could make a real difference in the quality and the quantity of life. It is an area of disparity for people with serious mental illnesses, and is responsive to stakeholders' interests and programs that will help with self-management around both physical and mental well-being.

There is a national advisory panel that includes the individuals that are affected, and also family members. There's a stakeholder advisory group that also includes peer support leaders. And there's interest at the state level as well because of many of the burdens of these follow-on state and local health plans in communities. So this is an important study that could really help a group of individuals that suffer disproportionately.

The fourth project is looking at a -- using a smart design, looking at how we might efficiently
and effectively, through federally qualified health centers, connect people with state resources in smoking cessation. So this study will look at the impact of what would be considered very pragmatic, sequential, scalable interventions that are aimed at the clinic, but also at the individual patient, to reduce tobacco use and tobacco-related disparity.

Individuals who are receiving their care in participating federally qualified health centers in a state and who smoke cigarettes and are 18 years are older, and who speak English or Spanish, will be eligible.

It is a three-phase smart design with four active interventions, each increasing, all quite small in intensity but each increasing if there is failure to respond to an early intervention.

The outcomes of interest will be the proportion of patients who enter quit-line treatment; smoking abstinence at 12-month follow up, including a sub-sample with biochemical validation; and the impact on health-related quality of life. And there will also be process evaluation of the
implementation of the system-level interventions that will be going out to patients.

It's an ambitious study. Thirty federally qualified health centers will be involved, with an anticipated enrollment of 6,000 patients. The duration of the active intervention depends on if the individual has responded because once they have responded, then they are no longer receiving the active intervention, so it's 6 to 12 months, going to follow up at 12 months. And it's a $9.8 million study.

We all know that the burden of tobacco-related illness is disproportionately now concentrated in those in lower SES populations, and that quitlines can bring both counseling as well as biochemical resources to bear.

So this is a pragmatic study to look at improving the reach of evidence-based treatments to the population most at need. And because it is trying to work with people in increasing opportunities, then the patient focus, we feel like, is strong and has been designed with input from
patient representatives from quitline experts and from folks across the state.

Finally, the fifth project is looking at the comparative effectiveness of two different modalities of delivering evidence-based treatments to children and adolescents who have anxiety in pediatric primary care. This is a very pragmatic question. It's come out of multiple stakeholders, saying that we know that cognitive behavioral therapy works, but we would like to have information that would suggest that various formats that make it more feasible and accessible are equally effective.

Children ages 3 to 17 who meet criteria for mild to moderate anxiety in diverse primary care settings will be enrolled and randomized to either online cognitive behavioral therapy in a series of programs that are already developed that are age- and developmentally appropriate, or to face-to-face cognitive behavioral therapy.

Some people say, "How could you have such a broad age range?" Well, it's possible because of these age- and developmental-specific modules. It's
also true that modified cognitive behavioral therapy has been shown to be effective in children as young as 3.

So the outcomes of interest will be anxiety symptoms. They will be gathered through both parent report as well as child report. Some research has suggested that children are more actuate in terms of reporting the impact of anxiety on their function. And then the second will look at how children report that anxiety is interfering in their life. We'll also look at parental outcomes -- depression, anxiety, and stress.

This is a two-arm randomized, controlled trial with a sample size of around 1800. The active intervention is delivered over a 12-week period of time, but this will provide the long-term outcome. So we'll get a sense of not only how well disease services work initially, but how well are they maintained over time. And that was an important attribute of this research that the community has asked for. And the total project cost is $13.6 million.
This is an area of special emphasis that we called out in our last PCS announcement, and should provide information that would be actionable to a variety of settings that deal with the very common issue of child and adolescent anxiety.

The outcomes are focused on those that are important to clinicians, patients, and parents. And parents have been quite involved in developing this study, including a Latino parent research committee at one of the site institutions.

So in summary, we're very pleased to bring to you five recommended projects today on behalf of the selection committee. The amount available was $52 million, and we came in really close, $51 million. Very pleased to have these, and I will turn now -- turn the podium back over to Gray to lead the discussion questions.

CHAIRMAN NORQUIST: So we're open for discussions. In this particular discussion, Larry Becker, Michael Lauer, and Bob Zwolak -- and now, I understand, Kathleen, you're also recused -- cannot participate in the discussion or the vote.
Ellen?

MS. SIGAL: Well, almost all these are areas I know very little about. So with that in mind, I just have two questions. Well, the tobacco one I know a fair amount about.

With the anxiety, how do you define anxiety in a child? I mean, there could be all sorts of issues with bipolar, all sorts of other issues. There could be induced anxiety because of abuse or — so I don't understand how you measure that without defining exactly what you're talking about. So that would be one question.

Then I have one on the tobacco because anxiety -- I mean, so what is it? I mean, how are you defining this so you can really measure it? Because there's so many different degrees of it. I mean, look at what's going on now all over the world. So what is it?

DR. WHITLOCK: Well, anxiety -- and hopefully this is better; sorry if it was a little fuzzy earlier -- anxiety disorders have criteria. And this is for children that meet criteria for an
anxiety disorder that is mild to moderate in severity. So they would need to meet criteria. It's not just the normal worry kind of situation. And the evidence suggests that anxiety disorders are increasing in children and adolescents, diagnosed anxiety disorders. So this is actually a problem. We often hear about depression and anxiety going tog, but we really have focused mostly on depression. When we talk to stakeholders, we talk to experts, we talk to clinicians, this is a very under-studied, under-addressed area that's causing a significant amount of suffering in children and in adolescents.

It's also important because the natural response of parents to anxiety -- which anxiety is fear or worry out of proportion to the circumstance. And the tendency in their child is to want to avoid. And the parent tends to want to protect the child.

So almost the natural instinct of parenting in those situations is to shield the child or keep them -- give them a pass from something that might be anxiety-producing. However, some of what's
necessary can be exposure-related.

So the point of that is that if not identified and addressed, this becomes a cumulative problem for children that can even end up in fairly disabling conditions as they go into young adulthood. So it's a serious issue, but it does have diagnostic criteria.

DR. WHITLOCK: Everyone knows way more about this than I, but sometimes the anxiety is reduced by the parents. So there could be issues -- I assume you're going to figure that out. So let me not take your time on it because Gray and others in the room know --

CHAIRMAN NORQUIST: Well, let me -- I assume, by what you're saying, Evelyn, is that these are children with DSM-V diagnosed disorders of anxiety, whatever those disorders are. But I assume that's the way they are, not just somebody comes in and says, "My child is anxious." They would have to meet DSM-V criteria for a disorder, I would think.

DR. WHITLOCK: And just to say one more thing because it was in your question, I think.
When we looked at this, there was a lot of -- we talked to the experts about, do we need to have -- know all the comorbidities and other issues like that?

And certainly, if you're doing medications, you would need to be very careful. In this instance, CBT is often helpful for a range of the other conditions and/or it's certainly not going to be harmful.

And it's also true that according to the experts, that even ADHD and some other things that are diagnosed can actually have anxiety underpinning and may even be misdiagnosed. So it's not contraindicated in those situations.

MS. SIGAL: On the tobacco -- yeah. Just the tobacco very, very quickly. There's so much going on in tobacco, going on at NCI, at the NIH, going on up through the American Cancer Society. I assume you have looked at the landscape, and this is something that is different than what is happening?

DR. WHITLOCK: Yeah. There is a lot going on in tobacco. However, this is almost at the
dissemination and implementation area, if you think about it, because this is really taking evidence-based treatment and looking at various strategies to try and efficiently, effectively, in low-resource conditions, connect people with the resources.

And so what will happen is the clinics will be intervened upon in various ways to remind them. And then the individuals themselves will be targeted in increasing ways to remind them of the opportunity. And so it's a pretty ambitious way to think about targeting a whole state, which is not necessarily being done in a lot of the other research.

And you're right, there is a lot of cessation research that's been done. But this is really trying to get at the interface to getting it to people.

DR. McNEIL: That was a grantee presentation. I had one question, and it relates a little bit to one of the comments that Bari Talente talked about with regard to MS. I'm talking about the grant with regard to a rare form of TB and our
desire to have two drugs versus three drugs, and the need for multiple institutions to participate to collect an adequate number of patients to get an appropriate sample size.

So here's the question. Without being totally intrusive, how do we know that the sample size is going to happen, and that some institutions aren't going to fall behind, and then the whole study will be sabotaged?

I worry about that in general for all rare diseases, and this one in particular, because a lot of the patients are going to be coming from poor neighborhoods in poor institutions that aren't necessarily going to have the capability of grabbing these patients and putting them in a study.

DR. WHITLOCK: Barbara, I don't remember if you were at the selection committee that day, but I think that was brought up by the selection committee, and we talked about being sure that we have a planning year in for this one to be sure that recruitment --

DR. McNEIL: I was there. I was just
bringing it up again here for everybody to hear.

(Laughter.)

DR. WHITLOCK:  Oh, good. Yeah. Because you're exactly right. This could go down because of inadequacies in the implementation. And so this is an instance where -- even though I think we're trying to move in that direction in general, this is an instance where we really need to be sure we do that so that we ensure that it's feasible. So thank you for that.

CHAIRMAN NORQUIST:  Okay. Then I think we need to move. I need a motion to approve this particular slate.

DR. McNEIL:  So move.

CHAIRMAN NORQUIST:  Barbara. And then a second.

DR. FERNANDEZ:  Second.

CHAIRMAN NORQUIST:  Alicia. Okay. So this is a vote by hand. All those in favor that are not recused?

[Hands raised.]

CHAIRMAN NORQUIST:  Okay. Anybody voting
against this? And I have to abstain because I may have a conflict. I'm not just completely sure. So Mary has advised me to abstain. Okay. It passes. Allen, are you on the phone?

DR. DOUMA: I am.

CHAIRMAN NORQUIST: Okay, Allen. How did you vote?

DR. DOUMA: I voted in favor.


DR. WHITLOCK: Okay. So this is also from Cycle 2 of 2017, from the targeted funding announcement, around symptom management for patients with advanced illness.

This was the first time we posted this targeted funding announcement, and we asked for studies that would look at long-term outcomes, at least six months, comparing evidence-based pharmacologic treatment with other management strategies for common symptoms experienced by patients with a range of diagnoses with advanced
illness and a life expectation of greater than six months. So we were trying to get not just the final four weeks of life, but a little bit more upstream in the palette of care process.

The priority research question asked that based on parent- and caregiver-centered outcomes both, what is the comparative clinical effectiveness of two or more approaches?

And we did define one of those being -- at least one being a pharmacologic intervention on any of the most common symptoms in patients living with advanced illness, so pain, fatigue, dyspnea, anorexia or cachexia, nausea, vomiting, and depression and/or anxiety.

Same merit review criteria from the other slate. We got 19 letters of intent for this. We invited 12. We received nine applications. And today we're bringing to you a recommendation to fund one out of the nine applications we received.

This is a project that's looking at personalized treatments for advanced medical illness, patients with depression, specifically with
heart failure. And it's a $2.6 million study. So the research question is looking at the comparative effectiveness of three treatment strategies for depressive symptoms in patients with advanced heart failure. So patients that have been admitted to the hospital with a diagnosis of advanced heart failure and who screen positive for depression are candidates for this study.

They can be randomized to one of three interventions: Either a behavioral activation, which is a short-term psychotherapy-type intervention that's evidence-based, combining the behavioral activation with appropriate antidepressant medications, or antidepressant medications alone.

The primary outcome is change in self-reported depressive symptom severity measured by the PHQ-9, but secondly, focusing in on important areas of patient functioning, health-related quality of life, global health, the caregiver burden, and then utilization as a representation of the primary disease as well as the depressive disease.
As I mentioned, it's three arms. It's a single-site, randomized, controlled trial, and the anticipated sample size, or the target sample size, is 450. And there'll be a 12-month follow up. As I mentioned, a cost of $2.6.

This is looking at pragmatic kinds of interventions that could be offered to patients who experience depression along with their heart failure. Because behavioral activation is more easily implemented than some other kinds of psychotherapeutic interventions, and a broader range of providers may be able to do this, further evidence here could be helpful for these patients.

And it looks at longer-term outcomes for patients and caregivers. It was developed with the input of patients who have experienced this situation, and will be managed with professional organizations and others.

So there's not more say about that except we fell somewhat short. And as Christine said, I can answer questions about that if you'd like to, at the end of this presentation or at the end of
presenting all of the slates. We were hoping to
receive more meritorious applications for this, but
we felt good about the study that we're bringing to
you today.

So let me stop there and see if there are
comments or questions.

[No response.]

CHAIRMAN NORQUIST: Yeah. I don't --
Allen, you're on the phone. Do you have any
questions?

DR. DOUMA: No, I don't.

CHAIRMAN NORQUIST: Okay. Yes, Joe?

DR. SELBY: Since you invited us, what are
your thoughts about the fact that -- I know this was
kind of a new effort. We kind of did in this one
what Harlan has been urging us to do for a long
time, which was to focus on symptoms.

And we didn't get more than one that we
felt we could fund. So I think it would be
interesting for the public to hear what your
thoughts are. And I would like to hear, too. I may
have already heard, but --
DR. WHITLOCK: Well, we are still doing a hypothesis generation around that both at the SC and the SOC. I think some -- and at the staff level. I think that some of the initial thoughts have to do with the fact that this was a first-time targeted funding announcement.

And sometimes it takes a while to get out to the right part of the research community. So we have wondered if giving a second opportunity, and maybe doing a little bit broader outreach, might be effected.

The second has to do with being clear about what we're aiming to target in this. It perhaps was off-putting by requiring a six-month or so longevity, if you will. Certainly we were trying to move out of the very end of life care, but it perhaps may have introduced some either discomfort or uncertainty on the part of the research community. So that's one possibility.

And then we wondered about the requirement for requiring a pharmacotherapy, although that's usually what people are given, and we wanted to
mimic situations where we were looking at pragmatic
alternatives.

That said, we think there's still room for
research in this area. It's really important. Very
patient-centered. And so we're thinking about how
we can give another opportunity, potentially, to try
and answer these important questions. But I'd
welcome thoughts from others as well.

CHAIRMAN NORQUIST: Christine, since you're
head of the selection committee, you may want --

DR. GOERTZ: Yeah. I really think removing
the requirement that there be a pharmaceutical
intervention will really open this up then and
increase the number of applications.

CHAIRMAN NORQUIST: Bob, did you want to
say --

DR. ZWOLAK: And I think I ought to add
that the SOC considered this and is enthusiastic
about reposting.

CHAIRMAN NORQUIST: Any other comments
about this particular one?

[No response.]
CHAIRMAN NORQUIST: Okay. No one is recused at this point, unless someone lets me know now. Okay. I need a motion to approve this grant.

DR. McNEIL: So move.

CHAIRMAN NORQUIST: Barbara.

DR. DOUMA: Second.

CHAIRMAN NORQUIST: And then a second from Allen. Okay. All those in favor, raise your hand.
[Hands raised.]

CHAIRMAN NORQUIST: And is anybody opposed?
[No response.]

CHAIRMAN NORQUIST: Anybody abstaining?
[No response.]

CHAIRMAN NORQUIST: Okay. Evelyn, I think you have two more. Is that right? There's the -- I see a medication-assisted treatment delivery for pregnant -- okay. And then another one, I think, after that. Right? Okay.

DR. WHITLOCK: Okay. So this is another targeted funding announcement from Cycle 2, 2017. And it also was the first time that this was posted, looking at medication-assisted treatment delivery
1 for pregnant women with substance abuse disorders
2 involving prescription opioids and/or heroin.
3
4 This targeted funding announcement was
5 focused on women with opioid use disorder, pregnant
6 women --
7
8 CHAIRMAN NORQUIST: Wait a minute. I'm
9 sorry. I forgot to ask Allen what his vote was on
10 the last one. It just dawned on me. Allen?
11
12 DR. DOUMA: Thank you. My hand is raised.
13
14 CHAIRMAN NORQUIST: Okay. Your hand is
15 raised. All right, thank you. I'm sorry. Okay.
16 I'm sorry.
17
18 DR. WHITLOCK: Okay. So when the SOC
19 worked on putting together this funding
20 announcement, there was a focus at that time --
21 there was a real growing understanding of the number
22 of women, and particularly newborns, being affected
23 by the opioid epidemic, and great concern about
24 getting resources to individuals, particularly those
25 that are in underserved situations.
26
27 So what we asked for was a CER that would
28 look at various ways of supporting the delivery of
medication-assisted treatment, which is an evidence-based approach, to reducing neonatal abstinence syndrome and poorer outcomes for the mother and the baby.

We were interested in very large randomized, controlled trials or well-justified observational studies. There are several states that have taken quite a bit of initiative because of the impact on their population. So we thought that there could be some good natural experiments.

We were interested in looking at what delivery models or components that had evidence of efficacy or were in common use, how they would compare to each other. And so we asked two questions.

The first is: What is the comparative effectiveness of alternative models to deliver comprehensive opioid use disorder treatment? And what is the impact on maternal and neonatal outcomes in pregnant and postpartum women with different levels of addiction severity?

And then the second was looking at
different mechanisms to support treatment delivery

to pregnant women that included more or less
resources for two aspects of medication-assisted
treatment, which is the induction of the treatment,
so coming down off of the opioids and then going
onto the medication, and then providing psychosocial
support. So this was -- and I want to make a
distinction that the second was really oriented
towards supporting providers in the delivery of this
service.

We received 18 letters of intent, we
invited 14, and we received 10 applications, and
we're proposing to fund two. These two address only
the first question, and we are discussing with the
SOC whether it is advisable to repost the targeted
funding announcement to deal with the second
question.

But these two applications that are coming
to you today from the selection committee represent
only the first two, comparing different models of
delivery for pregnant women with opioid use
disorder.

B&B REPORTERS
29999 W. Barrier Reef Boulevard
Lewes, DE  19958
(302) 947-9541
The first is a $5.3 million study called Moms in Recovery, looking at what is the optimal care approach for pregnant women and infants. And the second is the same population, but looking at a rural setting and different modes of delivering these services in rural Kentucky. They're each about $5 million.

The MORE study is looking at two different models of care. So one is an integrated model of care, where the office-based opioid therapy is delivered in the same location as prenatal care. The other is a perhaps more easily assembled referral-based treatment, where women with opioid use disorder in prenatal care are referred out to specialty services to deliver the office-based opioid treatment, and the impact of these different models of care on pregnant women with opioid use disorder and their infant in terms of outcomes.

So the two different models, as I mentioned, are really differing by whether or not they're at the same setting and whether or not they're integrated. The outcomes across these two
models of care will be -- the primary outcomes are the continuation of illicit opioid use, whether or not women stay in treatment, and whether or not there are perinatal complications, which would include neonatal abstinence syndrome. And that is a -- I'm sorry, that's a secondary outcome.

There's also a look at the impact of opioid use disorder on families. So there'll be consideration of whether or not mothers are able to retain custody of their children and quality of life.

This study is a prospective, observational, mixed-methods design, looking at two existing approaches. The sample size will be large, 2,000. And depending on the week that the women come in for prenatal care, the active duration of the intervention will range, but will go into -- from the third trimester or through six months postpartum. So there'll be treatment after delivery for women as well, and follow up through six months postpartum.

So this is a really important comparison.
because if it works as well to be able to refer to services and services are available, that's important to know since integration of treatment services can be something that can require novel organization of care.

This will also be able to look at a range of severities for specific subgroups, and to look at differences in outcomes, both for infants and for mothers, based on at least severity and other characteristics.

There will be a series of qualitative patient interviews to understand also how women experience the care and what is most acceptable to them. And the design of the study as well as the outcomes were actually informed by women, postpartum women who are receiving medication-assisted therapy.

There's a lot of interest in this type of study from the Medicaid medical directors and from others. And we have good networks, or the study team has good networks, that are involved that will help with both the conduct of the study as well as its dissemination.
The second study is looking at different models of support for women that are receiving office-based opioid in a rural site. The first will be -- and these are services to the woman, not to the clinician.

So the first additional support that women will receive is telemedicine consultations with clinicians who are experts in various aspects of the issues that women are facing who have opioid use disorder, so clinicians that are experts in substance abuse counseling, clinicians with expertise in maternal-fetal medicine, addiction medicine, and neonatology.

The contrasting condition will be additional support provided to women through in-person group sessions that are facilitated by a perinatal nurse and a peer support specialist. So we'll be looking at sort of an individual specialist consultation model through telemedicine versus in-person group facilitation and support.

The outcome here, the primary outcome, is treatment-requiring neonatal abstinence syndrome.
Secondary outcomes are some that look familiar and some that are a little different from the other study. One, custody status, is very similar; relapsed rate or continuation of illicit substance abuse; and then maternal mood and infant developmental milestones. Smoking cessation is also included in this one as an additional behavior that can affect perinatal outcomes.

This is a cluster randomized, controlled trial, the sample size is 1,620, and there will be 12 sites involved. And again, depending on when the women enter prenatal care, the length of the intervention will vary, but will go through six months postpartum.

So in a rural setting, the opportunities to provide additional supports to women are varied. But having different models that can inform practitioners and patients will be quite important because a number of women in rural settings need these kinds of support.

And the comparators and the outcomes were all based on focus groups with patients and
interviews with patients. And patients will continue to be involved through the conduct of the study. Again, there are numerous stakeholders involved because of the importance of the condition at a local and a state level, and those stakeholders will be critically important in helping to support the study and in disseminating its findings.

So in summary, we had $14 million made available. We have here two proposed awards that total $10.2 million. And I'll turn it back over for discussion and questions.

CHAIRMAN NORQUIST: Okay. So Bob Zwolak, you're recused from this. No one else at this point unless someone let's me know now. Any comments or questions to Evelyn about this one? Allen? Any --

DR. DOUMA: No, sir.

CHAIRMAN NORQUIST: Okay. Kathleen?

MS. TROEGER: Evelyn, just a quick question on project 2 in Kentucky. What's the plan for managing lost to follow up in that over the six months postpartum?

DR. WHITLOCK: I'm asking Steve. I don't
remember -- I don't remember any specifics about that. We always look at that. But I don't remember specifics. Do you remember, Steve?

STEVE: Well, these women will be -- are connected with these providers in the context of making this transition between the perinatal period and into postpartum. And they will -- they have relationships they've established with both these patients and physicians to try maintain relationships with these.

They have done similar kinds of studies before, with certain types of success. So we're fairly confident that they'll be able to do it. But I do agree. In general with this kind of work, this is a very challenging area to try to maintain contact with people that can easily move back into the system.

CHAIRMAN NORQUIST: Okay. I Need someone to make a motion.

MR. BECKER: So move.

CHAIRMAN NORQUIST: Larry. And a second?

MR. BARNETT: Second.
CHAIRMAN NORQUIST: Okay, Kerry. So I need hands raised of all those in favor.

[Hands raised.]

CHAIRMAN NORQUIST: Is anyone -- okay. Is anyone opposed?

[No response.]

DR. DOUMA: And I'm in favor.

CHAIRMAN NORQUIST: I'll get Allen. I'm just checking the room first. Abstaining?

[No response.]

CHAIRMAN NORQUIST: Okay. Allen?

DR. DOUMA: Yes.

CHAIRMAN NORQUIST: Yes. Okay.

All right. The final one before we take a break.

DR. WHITLOCK: Yes. Okay. And so this is between you and your break, so we'll go quickly.

So this is actually -- this is from Cycle 1, 2017. This was a targeted funding announcement looking at optimized multidisciplinary programs for nonspecific chronic low back pain.

And it was looking for large, randomized,
controlled trials or well-justified observational studies that would compare the effectiveness of optimized multidisciplinary nonsurgical treatment programs that were either combining evidence-based treatments or sequencing interventions for treatments -- or for patients with nonspecific chronic low back pain.

And you may recall there was a systemic review and clinical practice guideline recommending these nonsurgical, multidisciplinary approaches as kind of a first step. But a lot of uncertainty about combinations and sequencing.

The treatment programs, there is a large body of evidence on separate components. So we asked that any of the treatments that were in these combinations or in sequence were evidence-based and could be well characterized so that if the results were positive, the studies could be replicated and disseminated.

The priority research question was: What is the comparative clinical effectiveness of optimized multidisciplinary nonsurgical treatment...
programs involving combined or sequenced interventions for patients for nonspecific low back pain?

So we received 12 letters of intent for this targeted funding announcement, and we invited seven to submit a full application, and we received five full applications. We propose today to fund one of the five received applications.

This study is a $9.7 million study looking at optimizing treatment sequencing for patients with chronic nonspecific low back pain. This looks at two different evidence-based approaches. One is as the initial treatment. The first is physical therapy. The second is cognitive behavioral therapy.

So patients -- it's a smart design, and patients will be randomized to either initial physical therapy or initial cognitive behavioral therapy for those with chronic low back pain. The sample size is 945, and there are three study sites.

After 10 weeks, if there has been no response to the initial randomized treatment
sequence, then patients will undergo -- those that
are nonresponders will undergo a second
randomization. And they will be randomized to
either a mindfulness-based intervention or the
treatment -- the initial treatment that they were
not randomized to.

So if they were first randomized to CBP, in
the second round they could be randomized to
mindfulness or PT. So there'll a second level of
randomization that will create a number of different
groups, not just four different groups, but because
mindfulness is coming in as well.

The folks cannot have had any spine surgery
in the last 12 months, and they need to have an
Oswestry score greater than 24 percent and an
average pain rating greater than 4, which I think
puts them in a moderate-plus pain and severity -- is
that right? Yeah, moderate. So moderate-plus pain
or severity -- and they meet the definition for
chronic low back pain that the NIH has proffered.
Any age from 18 to 65 years.

The outcomes through 12 months will focus
on pain intensity and function, but will also look at a range of patient-reported outcomes around function, mood, sleep, social role, pain or interference, as well as long-term opioid use and healthcare utilization. And I mentioned the project cost is close to $10 million.

So because guidelines have looked and evidence has primarily looked at different discrete treatments, not looked at the sequence, there is a dearth of evidence about what to start with and how to proceed and in whom. And this research could be very helpful in taking these evidence-based treatments and developing some information about how well people respond initially and how well they do at various sequences.

This has been informed by patients and other end-use stakeholders, and the focus on multiple aspects of quality of life, which low back pain, chronic low back pain, can interfere, with is the strength of the study.

The investigative team is strong and has developed the approach in partnership with patients
and pain management experts. And those will be also helpful in dissemination.

So in summary, we were able to bring to you one study that we feel confidence about. It's a $9.7 million study on optimized multidisciplinary treatment programs for nonspecific chronic low back pain. And I will turn it back over for any questions or discussion.

CHAIRMAN NORQUIST: Okay. Questions? Comments? I don't have anyone recused at this point unless someone sees that they are. Francis?

DR. COLLINS: Just a quick question. So is it your impression that this $9.7 million will result in some kind of implementation opportunity?

DR. WHITLOCK: Do you mean will it be definitive evidence? Is that what you mean?

DR. COLLINS: Yeah. I'm wondering. I think it's a neat methodological study, and it certainly fills an evidence gap. But I'm just wondering. I'm harking back to this point in this conversation around implementation, whether this will result in some actionable opportunity for
either PCORI funding in this sort of low back pain.

DR. WHITLOCK: Well, This targeted funding announcement was the subject of a lot of discussion. And the whole area of chronic low back pain has been a challenging one. There's a huge need. A lot of questions in terms of research, but a real challenge in finding the next right study to do that would then change practice because so much is not -- we're not at that point where we can say a single study's going to do it.

So I would say, in answer to your question, the therapies that are talked about here are fairly commonly available. And if there were definitive evidence about sequences and in whom they work better -- because it's a fairly large sample size -- then I could imagine that that would be informative to the field and perhaps implementable.

I think that we're going to be creating evidence in this area for quite a long period of time before we have a lot of the answers, and one of the critical areas is going to be understanding how do we differentiate between the different types of
folks with chronic low back pain because we've got
them all in a lump together and they're not all the
same in terms of their pathophysiology.

CHAIRMAN NORQUIST: We'll hear from our
spine expert. Christine?

DR. GOERTZ: Yeah, hi, Francis. I think
that's an excellent question. I think that the fact
that the American College of Physicians, the FDA,
and the Joint Commission are now calling for non-
drug therapies before drug therapies for chronic low
back pain will help facilitate implementation.

Also, this particular study team is very
well-integrated into the physical therapy community.
And also, they have appointments -- the PI has an
appointment within the Department of Defense. So
there are a lot of -- I think there are more
opportunities for dissemination and implementation
of this kind of work than there has ever been in the
past.

CHAIRMAN NORQUIST: Any other questions? I
think always the -- yes, Larry?

MR. BECKER: I have a question. And I know
we've sort of covered this before, but as a non-clinician, non-researcher, the question that comes to my mind is we put $42 million out there. Employers have lots of low back pain issues. Insurers have the same thing. What is it that is keeping us from finding good projects to fund when we have this kind of money available to do this work?

CHAIRMAN NORQUIST: Christine, you want to -- because I know you're dealing a lot with this issue.

DR. GOERTZ: Yeah. We need to do better. There's no question. For whatever reason, we haven't quite hit that sweet spot. And I think that that's something that we need to continue to put more time and attention into in the path.

It's something that Evelyn and I have talked about because recently NIH put out a call for pragmatic comparative effectiveness studies to be conducted in the DOD and the VA. And we're planning to fund seven, and instead they had so many good applications that they funded 11.
So I think that we -- there can be lessons learned about the way that that announcement was both written and distributed that would be helpful, and that we need to -- we should not give up on this. We need to continue to figure out how to do a better job of putting together these announcements and getting them disseminated to the research community.

DR. WHITLOCK: Well, and just to build on what you were talking about, we were talking this morning. Harlan was talking about how funders could collaborate. And everyone has an interest in chronic low back pain, so we could be doing a lot more, and have started conversations with the VA and DOD and others around areas of shared interest. And this would be a really strong area, including the NIH collaboratory.

CHAIRMAN NORQUIST: Yeah. So those kind of topics are obviously something we should have more of a conversation about because it's not only in back pain. It may be in other areas as well. Right?
Okay. So any other questions or comments?

[No response.]

CHAIRMAN NORQUIST: So I need a motion to approve this. Bob?

DR. ZWOLAK: So moved.

CHAIRMAN NORQUIST: And then a second. Russell?

DR. HOWERTON: Second.

CHAIRMAN NORQUIST: Okay. So we'll go in the room first, then we'll ask Allen. All right. Everybody in favor raise your hand.

[Hands raised.]

CHAIRMAN NORQUIST: All right. Anybody opposed?

[No response.]

CHAIRMAN NORQUIST: And anybody abstaining?

[No response.]

CHAIRMAN NORQUIST: Allen?

DR. DOUMA: In favor.

CHAIRMAN NORQUIST: Okay. So it passes. And just on time. Perfect, Evelyn, as always. Okay. So we'll take a 15-minute break.
For those on the phone, we'll be back in about 15 minutes.

[Recess.]

CHAIRMAN NORQUIST: Okay, we're going to start back, Evelyn when you sit down we'll start back.

So the next session is about a targeted PFA development. Right. Okay. So, Evelyn and I guess Bob, Bob is on a call -- Bob will come back. He was on a call so I'll let you handle it.

DR. WHITLOCK: Yes. Okay. I don't see him on behalf of the Science Oversight Committee. Alicia is here. Would you like to say --

CHAIRMAN NORQUIST: Alicia, do you want to?

DR. FERNANDEZ: No, I don't --

DR. WHITLOCK: Just go ahead. Okay. So we are bringing to you for consideration a targeted funding announcement. Looking at the various approaches to psychosocial support and office-based opioid treatment for opioid use disorder and this is not the same as the medication assisted treatment in pregnant women, but it, it has some similarities.
So, we'll separate those out for you. Sorry. Let's see. Is that good? Is that better? Okay. Okay.

So this is just a reminder that this is a topic that has come through the prioritization pathway, and been developed for a targeted funding announcement. This is the summary we, I think provided for you in the brief, the Board brief materials supporting the rationale for this targeted funding announcement, but in brief, let me review it.

So, medication assisted treatment is first line evidence-based treatment for those with opioid use disorder. Buprenorphine which can be offered in a primary care setting as office-based opioid therapy is an important option for individuals because it has a wider range of individuals -- clinicians who can be trained and certified to provide it. So both a physician assistant and nurse practitioners, as well as MDs. It has a favorable safety profile and it is now available in a long acting form.

It's one of the areas that has been
emphasized in a number of recent announcements from the White House and others about expanding access to medication assisted treatment.

And currently a medication-assisted treatment by federal law requires the clinician to provide or refer adequate psychosocial services. It's also recommended through national guidelines that evidence-based psychosocial services be provided as part of office-based opioid therapy, but it's not clear from current evidence which services are better for which patients.

And in fact, when you look at individual trials and systematic reviews, there are mixed results on which psychosocial treatments are the most effective and even sometimes whether or not psychosocial treatments are necessary. The field has said perhaps it's because there was such robust comparator provision, but it's definitely mixed results in the available evidence.

And further, most of the evidence on psychosocial service support has been studied with Methadone and not buprenorphine.
Stakeholders across the spectrum are strongly interested in better evidence to inform the provision of a medication-assisted treatment and, and to support the ongoing expansion of access to medication -- to evidence-based medication assisted treatment.

So the question of interest that we're bringing to you for this targeted funding announcement today is what is the comparative effectiveness of psychosocial interventions versus standard medical management for patients who receive office-based opioid treatment with buprenorphine? Which psychosocial interventions are most effective and for whom?

When we talk to NIDA and we, we have spoken with NIDA and a number of stakeholders through the process of developing this, we were told that the question about how much is necessary for whom is the most important question around medication-assisted treatment right now, that really the barrier of not knowing how much psychosocial service support is necessary versus standard medical management is one
of the major barriers. So in this funding announcement, populations could include adolescents, patients with multiple comorbidities, ethnic and racial minorities. It doesn't have to include those, but these are populations that would be a particular interest.

The interventions and comparators would be standard medical management, and then a number of other interventions as listed here, all of which are evidence-based in terms of the context of medication-assisted treatment and the applicants would need to justify that the two competitors that they are proposing are evidence-based, that they can be protocolized, and that they therefore could be reproduced and understood in the context of the research.

The outcomes that stakeholders have told us are important are illicit opioid use, retaining people in treatment, how well people function -- particularly social role functioning; and then, ED visits, overdose, and an interesting outcome which is provider satisfaction. Providers are critical to
making these services available to people. And in fact, the adequate provision of these services can be a very positive experience for providers according to some of the stakeholders that we spoke with.

So understanding the best ways to support providers in supporting patients in these interventions is one aspect of the research. The timing should be at least one year of follow-up and this would be focused on outpatient clinics and practices were office-based, opioid therapy is offered.

We recognize that there's been a fair amount of investment in opioids across the spectrum from prevention to this aspect which looks at the treatment of opioid use disorder. And so, the requested commitment here is modest compared to some of our other targeted funding announcements. We believe we could get four to five well-constructed studies for a total direct cost of $4 million and up to $25 million in total costs and we would specify that the maximum project duration would be four
And so, I bring this to you for your consideration today. Bob, I don't know -- you were out of the room. Do you want to add anything to this?

DR. ZWOLAK: I do. Thank you. I apologize for coming in late.

In discussing this particular next step and in our funding for opioid disorders, the SOC had a robust discussion about how much we've spent at this point, something just shy of $74,000,000, 13 large projects at various stages of trying to break the cycle of opioid use from preventing a potential new use from early stage use and from this stage which we funded, four studies would be people with opioid dependence, but it's, as we all know, it's a huge problem. Forty -- 42,000 patients died from opioid use disorders in 2016. That's more than everybody in my entire hometown, dying from opioid use disorder.

So it seems like an obvious and very important step for us to take.
So the SOC in endorsed this enthusiastically after reviewing what we've sponsored to-date.

DR. WHITLOCK: Thank you.

CHAIRMN NORQUIST: Other? Larry. Did you want to? Yeah, go.

MR. BECKER: So, you know you read about opioid issues every day in the newspaper. This is a huge problem. It's a four year study. Have we done the work to say who else is doing what? And this is it to make sure this is not redundant?

DR. WHITLOCK: Well, we -- I'm trying to remember if we went to ClinicalTrials.gov, I think we did, to look at what's being done. Can you remind you? Do you remember?

DR. ZWOLAC: In fact, much of that is in the written materials for this.

DR. WHITLOCK: Yeah, I think we went to ClinicalTrials.gov and we've actually been in contact with NIDA the whole time in putting this particular proposal together, as I mentioned, sort of in passing, the opinion that we got from one of
the chiefs in NIDA who actually sees these patients, he's a psychiatrist, was this is the question to answer right now around medication-assisted treatment. And, as you are probably aware, we didn't show all the background, but as you're probably aware medication assisted treatment is now being called for in a lot of situations.

So we would allow large, observational studies that could potentially get to an answer more quickly if they can be proposed, but we don't think that this will be duplicative and we think it's really important.

CHAIRMAN NORQUIST: Other questions or comments? Yeah. I think the key issue Larry is that NIDA was -- they will know what's out there. And I think one of the common things that people think is you just give buprenorphine and that's it and it works; and that doesn't work at all. We have a buprenorphine clinic at my clinic, so we've had a number of issues.

I would just stress that under-resourced populations are really critical for this because
they're the ones who have many of the problems and
that's been our experience without any other
intervention. Just giving buprenorphine doesn't
work. Alicia.

DR. FERNANDEZ: Thank you for that comment, Bob. It's something that we also fought a little
bit about on the Science Oversight Committee because we are doing great work in opiates. This is
actually a really important study as Evelyn and pointed out.

We really want to be sure to hit multiple
populations. So, for example, we've done the rural
Kentucky Now with the pregnant women with opiate
dependence and that's a hugely important study, but
at the same time we also wanted to hit some of the
traditional urban underserved populations.
Particularly who might have more access to
buprenorphine through all sorts of systems of care
where figuring out how much more is needed will be
key in terms of psychosocial support. So we didn't
end up -- I think putting that into the program
announcement, but we are struggling with ways to
call it out and saying that we are specifically
interested in traditional -- additionally in urban
underserved.

Is that right?

DR. WHITLOCK: That's right. And I think
the other thing I'd like to say is we had some
extraordinary -- extraordinarily helpful input from
stakeholders. And the concept that was talked about
pretty strongly is the idea that the amount of
psychosocial support and the nature of psychosocial
support should be needs based. And that it might be
most effective and efficient to think about stepped
down care rather than stepped up care, particularly
for some of these vulnerable populations, but that
people who have opioid use disorder, some have
quite, quite good maintenance of their social roles
and social functioning and some have lost almost
everything.

So those folks may have different resources
to bear and it would be very important to
understand, you know, how to target the services to
support people at various -- with various needs.
CHAIRMAN NORQUIST: The only thing I would say in particular in some of these populations, I deal with them all the -- you know patients all the time, is that there's also comorbid substance abuse. The assumption that you're only using opiates is not true.

There's a lot of use of cocaine in addition to that, so it gets very complicated.

DR. FERNANDEZ: I picked up on that as well. And we can have a conversation to make sure that when the announcement goes out it, speaks about that.

CHAIRMAN NORQUIST: Allen. And now I understand Harlan has magically appeared on the phone, no longer in the room. So, did either one of you have any comments or questions about this?

DR. DOUMA: I don’t.

DR. KRUMHOLZ: None for me, thanks for asking though.

CHAIRMAN NORQUIST: All right. What do we do? A hand vote? Yes. Okay. So I need -- well first I need a motion. Thank you. Barbara. And a
second? Thank you Gail. Okay. So all those in favor raise your hand. And is anybody opposed? And anybody abstaining? And then Harlan, you're vote?

DR. KRMHOLZ: For.

CHAIRMAN NORQUIST: Okay. And Allen?

DR. DOUMA: I'm in favor.

CHAIRMAN NORQUIST: Okay. So it's approved. Thank you Evelyn. Evelyn, I think that's your last presentation to us in person, is that right? Thank you very much.

[Applause.]

CHAIRMAN NORQUIST: We may find some other time to bring you up and torture you, but anyway, that's all right. Okay. So next. Are we ready? Is Adrian? If not, we can -- two blocks away.

DR. SELBY: We're done a little early.

CHAIRMAN NORQUIST: Do you want to go Joe and do your approval.

DR. SELBY: It would be a lot better to do it in the sequence that -- if they're two blocks away,

CHAIRMAN NORQUIST: Two blocks away and
then parking. Do you want to bring up something else? I mean, we have, I don't think it's two blocks away means 5 minutes.

DR. SELBY: Why don't I do the PaCR Awards? I think that would be --

CHAIRMAN NORQUIST: The PaCR -- okay.

DR. SELBY: It’s toward the end.

[Side discussion.]

CHAIRMAN NORQUIST: That’s what Joe’s talking about.

DR. SELBY: I have another one I'm also presenting.

CHAIRMAN NORQUIST: What else --

DR. SELBY: -- as part of their presentation --

CHAIRMAN NORQUIST: No, I'm talking about the awards, your 4:45 thing. Yeah. So for those on the phone, we're jumping ahead to our people for the 3:45 session on the PCORnet update are not here yet. So we're moving that to 4:45 session that Joe was going to do on the PaCR awards, Partnerships to Conduct Research within PCORnet.
DR. SELBY: We’re -- look around 128.

CHAIRMAN NORQUIST: There you go.

DR. SELBY: Okay. Thank you Gray. There's some small advantage here and that is that we are still in kind of the slate mode. So I am presenting a slate now. I'll ask Christine first --

CHAIRMAN NORQUIST: Wait, no. Those recused from this one are Christine, Alicia, and Barbara.

DR. SELBY: Oh, you’re recused.

DR. DOUMA: Okay.

CHAIRMAN NORQUIST: So the three people: Barbara, Alicia -- no, no. You don't have to leave, you can’t be in the discussion or vote. Yeah.

DR. SELBY: Do you want to say anything to kick this off? Okay.

All right. So, in collaboration with Leah, who chaired the Selection Committee for this discussion, I'm happy to bring you a slate of awards that are under the title of partnerships to conduct research within PCORnet, otherwise known as PaCR.

And now -- okay. So this was a funding
opportunity that was directed to PPRNs within PCORnet. They had to be the primary sponsors. They had to bring collaborators, but they had to be the prime sponsors and it was seen as a major step in our multipronged strategy to achieve a sustainable, national research infrastructure and with particular attention to the role of PPRNs within PCORnet.

There were four distinct requirements that these PPRNs had to meet as they applied. So we had some -- each one of them aimed at strengthening the likelihood of sustainability. The first is they had to come with external partners, so there had to be some co-funding, either direct dollars or in kind support from outside funding organizations. These could be pharmaceutical or device manufacturers. They could be foundations, large patient advocacy organizations or other foundations or they could be healthcare systems, but they had to bring and specify the nature and amount of co-funding and it had to be at least 20 percent of the PCORI contribution.

The second requirement was that it had to
advanced data integration. Single PPRNs by themselves were not really, exactly a PCORnet network type of project. So we required data linkages. These could be linkages to CDRNs, they could be linkages to registries. They could be linkages to other PPRNs. They could be linkages to patient reported data, but they had to expand and link data as part of the project.

The third was they had to be legitimate high quality, highly relevant comparative effectiveness research studies. So this was -- there's nothing demonstration about them, there's no points given for this being a demonstration. This had to be competitive, comparative effectiveness research, and to the maximum extent possible they had to leverage existing PCORnet resources like the coordinating center, particularly like the common data model, possibly like the health plan research network partners or other CDRNs or PPRNs.

So the Board approved the development of this PFA in June of last year; and again, with thanks to a Merit Review for moving this through.
Here we are 10 months later with an approved slate. The funds available at the time or up to $21,000,000.

These are these standard research review criteria that Evelyn presented. And I just wanted to show you how data linkage components and leveraging existing PCORnet resources were built into the scientific merit criterion. And the external partnerships and co-funding were built into the patient and stakeholder engagement criterion. And that's how the Merit Review reviewers were instructed to score these.

I will say that they -- that all of these and perhaps because they were led by PPRNs did an amazing job on engaging patients in their own organizations in developing the research ideas and in planning engagement, as well as dissemination throughout and after the projects.

Again, the same format here. Sixteen, LOIs were received, 14 were invited to submit full proposals. And remember this was a limited competition among 20 PPRNs. Ten PPRNs submitted
proposals and out of those we are proposing to fund four.

And these are the four. I won't say too much about them here because I'm going to introduce them separately. I will say that three out of the four have to do with pharmacotherapies. I will say that the first three are clinical trials and the fourth one is a large observational study. And I will say that the amount of money here adds to just under $21 million dollars -- over 20.

So this is the first one. This is a comparative effectiveness study of using pharmacogenomics to guide the treatment of depression. So these can be either newly diagnosed patients with depression or patients who have failed one or more previous therapies, but major depression. So what is the comparative effectiveness of combinatorial pharmacogenomics-guided treatment. This is an available; covered by insurance and Medicare diagnostic test, 12 gene test. Some of the genes measure actually does the treatment work in people with this version of the
genetic marker, so-called a gene treatment interactions. Some of the other genes have to do with how drugs are metabolized and help steer toward or away from particular therapies that may be over or under metabolized.

Patients that are eligible are patients that are 18 to 65 years of age with a major depression diagnosis and they're referred by a network of 80 psychiatrists based within four PCORnet CDRNs. So you get the idea that this PPRN, which is based on mood disorders reached out to four CDRNs to actually attract the patients and created a network of 80 psychiatrists. The intervention is the pharmacogenomics-guided treatment and the comparator is following a 2016 state of the art depression treatment guideline. And the primary outcome of interest is the WHO (Five); patient reported wellness. The secondary outcomes include other patient reported measures and a novel, mobile health application. It's based on a cell phone and it measures depression by measuring things like the number and length of phone calls, text messages,
movement around in space during a day, and also
certain aspects of the intonation of one’s voice,
but nothing to do with the content of what one is
saying.

The sample size, this is a individually
randomized controlled trial. The sample size is
400, 200 per arm. The intervention goes for a year
and the patients are followed throughout that year.
And the total cost is $4.8 million.

The two external partners include the
pharmacogenomics lab, which contributes the tests as
well as the analysis and the training of clinicians
in the interpretation. They have a very nice
product which helps guide clinicians in going toward
or away from any of a number of antidepressant
candidates. And the second external partner is the
manufacturer of the m-health application and they
provide the platform, the license implementation
services.

The project also meets the criteria of
advancing data integration by combining patient
reported outcomes, intense usage of the common data
model from the four CDRNs, the pharmacogenetic data
and the mobile health data, and it uses the common
data model, the PCORnet coordinating center, as well
as the four CDRNs and the one PPRN.

The impact here is in our judgment, both
very patient-centered and high. This actually looks
at how a diagnostic and available and covered
diagnostic tests works in the real world. There are
clinical trials which suggests that this a markedly
increases the initial rate of response and improves
a patient reported outcomes compared to -- not using
pharmacogenomic testing, but it has not been tested
in a real world clinical population. It is a
patient-centered in that it directly addresses the
question of how to get to more personalized,
effective treatments sooner and also is heavily
based on PROs selected by patients from this PPRN.

The dissemination as I said, includes -- is
extremely good and I'll just leave it at that.

So that's the first study. If there are
any specific questions about this one, I could
answer them now or I will move forward to the next.
Okay.

So this second study is a study of children with limited juvenile idiopathic arthritis, which is the largest cause of autoimmune inflammatory arthritis in children. So much looks much like rheumatoid arthritis, except that the rheumatoid factor is negative. Limited means that at diagnosis these children have fewer than five joints affected and the question is, does early initiation of a biologic agent in this case, Abatacept, prevent disease extension in children with new onset limited juvenile idiopathic arthritis compared to standard guideline treatment which is initially non-steroidals and articular injections as needed.

So population is children two to 16. They have to be detected within six months of the clinical diagnosis and have to be have four or fewer joints affected, must have active disease in at least one joint. They are being recruited by a network of pediatric rheumatologists who are already affiliated with a large national registry that as the children are identified and recruited, they are
recruited into the registry and also into this trial. If they join both the registry will collect a large amount of ongoing follow-up data over a period as long as 10 years. So we'll have long-term follow-up in these children.

The intervention is usual care plus Abatacept; 24 weeks of Abatacept. And the comparator is the usual care alone. The outcome, the primary outcome is a progression. So a child with less than five joints affected progresses to having five or more joints affected and/or the incidence of inflammation of the uvea, so uveitis.

And the secondary outcomes include several patient reported outcomes related to global health, functional ability, pain, fatigue, depression, and others as you see there, but the primary outcome is in fact progression.

This is also a randomized controlled trial. This is a fairly rare condition. The sample size is 306 patients per arm, and the intervention goes for 24 weeks. So you take the Abatacept for 24 weeks and then you stop. So this is not the initiation of
long-term Abatacept. Follow-up is 18 months and the
cost is $7 million.

The partners, there's three external
partners here. One is the pharmaceutical company
which is contributing, study drug and also
contributing support for some ethnographic work
that's being done to better understand and enhance
recruitment of these children and their family
members. A patient foundation is also engaged and
they are very actively engaged. They provide
personnel, data sharing, help develop patient and
caregiver dashboards and treatment algorithms and
they're also very involved in dissemination. Are
prepared to be very involved in dissemination post-
study.

And the third is the disease registry,
which provides personnel and technical assistance in
maintaining the data warehouse, the software
modifications, and actually long-term follow-up.

The data integration, obviously then
included the registry, the electronic medical
record, and the survey data. I should say, one CDRN
is involved in this study as well. So it's seen as an alternative source of recruitment and they've engaged the rheumatologist associated with three sites within the CDRN. The common data model and the coordinating center are both involved.

And the impact here goes actually beyond rheumatology. So these days in autoimmune diseases, this idea of hitting people with new onset early, early in the course of an autoimmune disease with a potent biologic may have long-term benefit in either preventing progression or even altering the progression of the disease so it may be relevant not only to inflammatory arthritis, but also to, for example, inflammatory bowel disease. There's also, and this is a comment from the reviewers who were very excited about the heterogeneity of treatment effects analysis, which was based on disease severity.

So it may not be that all the children benefit from this early aggressive treatment, but perhaps the more severe children do.

Again, patient-centeredness. This was far
and away the question that patients and particularly
their parents were most profoundly interested in.
This is the question they brought forward. They
would love to understand that there was something
they could do early to prevent or slow progression.
And again, outstanding engagement through
the PPRN and also through the registry that's
associated.

So that's the second project. And I'll
just ask -- yes, Larry and then Barbara.

MR. BECKER: So what are the rules of the
road around the partners? In other words, and just
sort of pick on pharmaceuticals here.

Do they have any rights to a non-publishing
or you know, if the study doesn't come out because
it's their drug -- doesn't come out in their favor,
you know, what are the rules of the road here?
Because we've had this thing where we say we're
going to publish everything good, bad or
indifferent. What are their rules of the road with
these partners that they pick up?

DR. SELBY: Okay. So first of all, we rely
extensively on the institutions and in the contract we let them know that we rely on the awarding institutions to have these safeguards against these types of conflicts. So that's first and Mary sort of briefed me on this, to have conflict of interest policies in place. Yes.

SPEAKER: [Off microphone.]

CHAIRMAN NORQUIST: What are you asking?

[Off microphone discussion.]

DR. SELBY: No, absolutely not. No, no.

DR. LAUER: Larry, these are all funded on our funding agreement, which of course requires that results be publicly made available. They're subject to all the same requirements as all our research studies. They'll be peer-reviewed, they're subject to our conflict of interest requirements, and these will also have additional conflict of interest requirements related to the co-funded activity.

MR. BECKER: What got me to thinking about it, it was early in your discussion, you talked ten-year follow-up on the registry. I'm thinking, well, ten years from now, who knows, and that's what made...
me think about that. Okay.

DR. SELBY: I think you're absolutely right to point out, this is the first time -- we have a few studies where pharmaceutical companies have provided drug before, but this is the closest we've come to co-funding studies with pharmaceutical companies, so it's very good question to ask. Barbara.

DR. McNEIL: Two questions. The first is, since this has a small number of patients, I'm assuming there's a pilot study to show that the groups can do a run to get the correct number of patients?

DR. SELBY: All of these studies, all four of these studies will have that. Will have a period built into the contract where we assess whether they actually can go forward.

DR. McNEIL: Okay. And the second question is, I'm a little surprised, and maybe Ellen could talk about this, that this isn't a study that the FDA has already looked at as part of their initial approval.
DR. SELBY: There has been a study in early rheumatoid arthritis, so a study somewhat like this, but a much more less of a real world clinical trial. And so, it has appeared --

CHAIRMAN NORQUIST: Wait, wait. I just realized. Barbara, you're recused from this. You cannot have a conversation. Thank you. I completely.

DR. McNEIL: Sorry.

CHAIRMAN NORQUIST: Let’s remember Christine, Alicia, and Barbara are recused from this.

DR. SELBY: Can I, is anybody else curious about the answer to the question?

[Laughter.]

CHAIRMAN NORQUIST: I'm curious. Go ahead. I’m not recused.

[Laughter.]

DR. SELBY: So this has been studied in a smaller clinical trial already and that may have had some FDA involvement. I'm not sure. There is an IND for this study, but they are not, they are not
seeking a -- what they've told us is that they are not seeking a change in indications. They feel that this is so closely watched by the rheumatology community that if the study is positive, it will take off on its own.

So they are not seeking a change in indication.

DR. SIGAL: So why are they not requesting a label change?

DR. SELBY: I think it's because they, my understanding from what the investigators told us was that they -- this is a burning question in rheumatology right now and they feel like it's not essential to get a label change if the study shows that in fact it works, that it will be picked up very quickly without that.

DR. SIGAL: Well, that gets into another whole issue that's a big mess. But the problem is you've heard Scott and Janet and we've been working on label indications and updating labels, but if in fact this is positive and there’s data, in fact, there should be label indication on this because
that will have changed practice.

In rheumatology, particularly in cancer, we have -- we can debate about NCCN guidelines and ASCO deadline guidelines, but we have a lot of professional societies, though this kind of infrastructure I’m told, does not exist in rheumatology. So they’re very one off. So I, you know, it’d be interesting to see the intent.

DR. SELBY: We can definitely. -- we can definitely, as we negotiate this, we can definitely follow-up with them and get clearer information on exactly what their thinking was about why to not go forward at this time.

DR. SIGAL: Yeah, because this is already an approved agent; right?

DR. SELBY: Yes.

DR. SIGAL: So this is not a registration but maybe a new indication. There must be some reason for them to do this. It is important research, but it is a little -- some things are a little bit odd about it, but if it is a positive study, one would want and expect a label change.
DR. SELBY: Good.

CHAIRMAN NORQUIST: [Off microphone.]

DR. SELBY: Okay. We'll go on into the third study. Now this, you have to completely change your mindset because this is a totally -- this is not about pharmaceutical, this is not an individual -- well, one of these two trials is individual level trial, but the primary study is a system level intervention. This is about a national program to help delivery systems improve blood pressure control in their entire populations.

It is a program that's been put into place by a large national, physician organization which will go unnamed, and a large national disease focused -- cardiovascular disease focused organization which will go unnamed.

So the first trial we call the Clinic RCT or clinic trial. This compares how to do this, how to roll out this program of blood pressure control to clinics and institutions. So different clinics in institutions will do it somewhat differently, but basically it benefits from having data from having
champions from disseminating guidelines. We're working on both a patient adherence to drugs and what's called clinical inertia. That is the reluctance of physicians to augment a treatment in the face of poorly controlled blood pressure.

So in this trial -- well that's -- let me just say what the Device RCT is now and then I'll get back to the precise intervention.

The device trial compares home blood pressure monitoring with a standard home blood pressure cuff to home blood pressure monitoring with a standard cuff that is Bluetooth enabled so that it can prepare enhanced reports of blood pressure levels over time for the patient and for the patient's physician. So standard cuff versus Bluetooth enhanced cuff with reports.

So the study population is in the Clinic RCT. These are willing clinics from two PCORnet CDRNs who have said that they have multiple sites who would be willing to participate in this program, this national program of blood pressure control improvements. All adults then are considered,
they're not reached out to or approached. They are simply the denominator of the rate, which is the outcome that is blood pressure control. And all adults who have had at least one outpatient encounter with a diagnosis of hypertension in the past year.

And the population in the device randomized control trial actually comes from four CDRNs and these are adults who have blood pressure that is not well-controlled and have at least one ambulatory visit and who own a smartphone, because a smartphone is part of the receiving the Bluetooth reports.

So the intervention and comparator. In the clinic trial, the intervention is full support which means sending a practice facilitator to the sites. So this is a question that's of relevance to the national physician and patient advocacy organizations. Do they need to actually put boots on the ground and have people show up in these clinics to work with clinic staff or is the less, expensive, less invasive self-serve support method, which is a combination of printed materials and an
orientation webinar for program staff? So two levels of intensity of this program intervention. The device trial is again the Bluetooth enabled blood pressure cuff versus the standard home blood pressure monitoring cuff.

So the outcome of interest in the clinic trial, it's simply the proportion of patients who are in control of their blood pressure among all patients with a diagnosis of hypertension at each of the clinics and for the device trial it's did the patient -- so remember in the device trial these patients have been recruited, their clinicians are contacted, so you know the individual blood pressure target. And so, it's did they obtain blood pressure control?

Secondary outcomes are numerous including the magnitude of the blood pressure reductions and a measure called the measurement quality index, which is a proportion of clinic visits with at least one uncontrolled blood pressure reading, the therapeutic inertia index, a measure of it, and the adherence index, which are measures of clinician and patient
adherence.

Study design is a cluster randomized trial in the clinic trial and individual level randomized trial to study the device. Twenty clinics are randomized, ten to each arm in the clinic trial, 2,000 patients are randomized, 50 percent each in the device trial. The clinic trial has a duration of 18 months and the device trial a duration of 12 months. And follow-up is also at 18 and 12 months respectively. And the total project cost is $6.5 million.

The external partners in this include those two entities, the very large disease advocacy or cardiovascular disease focused organization and they're contributing personnel, overall study support, and travel expenses. And the same can be said for the very large physician advocacy organization. And the total contribution from them is $1.5 million. A common data model is extensively used to calculate all of these measures of blood pressure control in both studies; in the clinic trial and also in the individual level trial.
There is also patient reported outcomes in the blood pressure control trial in the device trial and data from the device that's integrated. And again, the coordinating center, as well as the common data model as well as four CDRNs. And one large PPRN are involved in this. Smart IRB is used. And also one collaborative research group, the Cardiovascular Disease Collaborative Research Group is heavily involved in this proposal.

CHAIRMAN NORQUIST: Larry.

MR. BECKER: I just have a curious question and that is, is the question of blood pressure accuracy at home readings versus clinic readings a settled question.

DR. SELBY: You know you could probably ask the next speaker after me, Adrian, but I think what is known is that home blood pressure measurements are better predictors of heart disease outcomes than clinic reported blood pressures, which would tend to say that home blood pressures do as well or better at capturing a person's true blood pressure. The true variable that matters.
DR. DOUMA: Joe.

DR. SELBY: Yes, Allen.

DR. DOUMA: A couple of questions related. How does blood pressure control differ from attainment of individual blood pressure goal? And part two --

DR. SELBY: The latter would be just a little more patient tailored. The individual level control might be, for example, if the person was elderly or if they had diabetes or if they had kidney disease, they may have a different goal than somebody who was not. And this would be worked out with the clinicians, so the clinicians are a part of this trial and otherwise you'd take standard recommendations and you apply them to the entire population.

DR. DOUMA: But why wouldn't, why wouldn't we do that -- individualize blood pressure goals for both the device trial and the clinical trial? Why change it?

DR. SELBY: Because we're not talking -- the first one is completely electronic data study
and so you don't know what the physician and the
patient have agreed to.

DR. DOUMA: Okay. And do we have any
concerns about having blood pressure too low? So if
somebody reaches there, they attain their goal, but
there are too low.

DR. SELBY: You know, I don't think that
was addressed. It's not a large problem. It's not
like blood glucose control, which is to well-
controlled sometimes. Mike, if you want --

SPEAKER: One thing that was interesting
even though the blood pressures that were attended
were very aggressive, there didn't seem to be harm
from bringing the blood pressure down “too low.”
That's not the problem. The problem is that we
can't get the blood pressure down low enough.

DR. SELBY: Okay, I'm going to move on. If
there are no other questions, move on to the fourth
project. Now we're switching to, for the first time
an observational study. So this is -- part of it is
a big data study and part of it is an observational
cohort study that actually involved identifying and
recruiting patients but not randomizing. So this is a little complex because there are two diseases. What I say about one is, is very similar to what I say about the other, but there's a Crohn's Disease study and an ulcerative colitis study. This comes from our Crohn's and Colitis -- the PPRN, which includes patients with those conditions. And the question in each case is what is the comparative effectiveness of second line biologic agents? And the comparison is between two that are used in this disease and Crohn's disease, Vedolizumab and Ustekinumab among patients who are either non-responders to initial therapy with anti-TNF alpha drugs or who have become non-responders overtime, who's response has failed.

So about 30 percent of patients, all patients fail to respond initially and over 50 percent of those who respond initially ultimately reach a point where they no longer are responsive. And that's true in both conditions. So you can see that it's the majority of patients with each condition who will at some point in their experience
of the illness will be eligible for this study.

The ulcerative colitis study is a very much the same except that the Vedolizumab is used again and the other agents is this time of small molecule called Tofacitinib. These are adults, and as I said, they are people who have been nonresponsive or lost responsiveness to the initial biologic, which is anti-TNF alpha. And I've already gone through the interventions for each. Both our studies in a new users. So in both of these cases electronic data are used to identify people just beginning -- just a starting these agents.

So in the prospective cohort study, and it's true for both Crohn’s and Ulcerative Colitis, patients are being recruited from two of PCORnets health plan research networks, and also from a very large national multicenter cohort of people with adult IBD at the time they start one of these agents. And longitudinal collection of clinical and patient reported data is then conducted following the initiation of their agent. And this longitudinal data collection uses among other
sources, the PPRNs portal. So the large PPRN has a portal and a survey system that will be used to collect the patient reported outcomes.

In the retrospective study, this is based completely within the health plan’s data and there patients are followed for continuation of treatment for hospitalizations and for surgery. So that there’s no patient contact in this retrospective cohort study.

The sample sizes in both Crohn's and Ulcerative Colitis. The perspective study will have 382 patients. That's an estimate of at least 382 patients. And the retrospective study, the estimate is it'll be nearly a thousand patients with each condition. And the outcomes in the prospective study, it's a battery of patient reported outcomes related to pain interference and fatigue six months after treatment initiation also, whether they were able to continue their treatment for at least a year. And the secondaries are more domains of PROMIS instruments related to sleep disturbance or dissatisfaction, anxiety and depression, and a
symptom index.

And again, in the retrospective study, the only outcomes are those that can be collected from a secondary data. So all cause hospitalization, need for abdominal surgery, and the persistence or treatment at one year. The prospective study is a 26 weeks in duration. The retrospective study is a year in duration. And total project cost is $2.4 million.

The external partner is the foundation that sponsors the PPRN and they are contributing a $820,000 in the form of a patient engagement work and support of the cohort, and the PPRN itself. The integration is met by integrating clinical data from EMR's claims data and a patient reported outcomes data, I shouldn't say clinical data from health plans, not EMRs and patient reported outcomes. Two PPRNs are involved, two health plan research networks, and the coordinating center.

And the impact here is essentially these are relatively new agents and there's very little known about the relative -- and they are expensive
agents, very little known about the comparative
either effectiveness or side effects of these new
agents. So this is really an early look at how
these agents perform in real world settings for
patients who have failed first line treatment or
stop responding to it. It's a knowledge gap that
patients were very quick to point out, highly
prioritized by the patients in the PPRN, and the
outcomes were selected by patients. And again,
thanks to the PPRN a really strong, engagement plan
and dissemination plan.

So any questions about this observational
study? Yes.

DR. McNEIL: So --

CHAIRMAN NORQUIST: Barbara you’re recused.

DR. McNEIL: I’m recused, oh my goodness.

So can somebody asked my question?

[Laughter.]

DR, SELBY: One thing that's not on here, I
just wanted to add is that these are observational
studies and they have recruited a really world
class expert in causal inference in observation
study designs to help manage this one, so it didn't make it to the slides, but it's true.

MS. HOLE-MARSHALL: I just wanted to say this is the first time the Selection Committee has seen these group of studies through the targeted PCORnet and it was really a pleasure to get to listen to them and to see some of our processes starting to mature in that way and I know it took a lot of work on staff time to get these into our cycle. So for those on the Board that aren't in the details of some of those processes, these are the first time you're seeing studies that have come through Merit Review as well as our other processes that we use for selection and it was great and we look forward to continuing to work on that too.

DR. SELBY: Yeah, thanks.

CHAIRMAN NORQUIST: Thanks Leah. Anybody else? Bob?

DR. ZWOLAK: So I have a comment and kind of a blue sky question, the comment is I really support testing these small molecules. I think they have the opportunity for significant
breakthrough in these people with this terrible inflammatory bowel disease and Crohn's, which can be just an awful disease. The blue sky question is, is there a 20 PPRNs, we're funding for these -- what does this say about the fate of the other PPRNs and there weren't even that many. There are 20 PPRNs, there weren't even 20 applications or only something like 20 letters of intent and 14 invitations and then 10 applications. What does it say about the health of the other PPRNs?

DR. SELBY: Great question. And thanks. First of all, I would say we were, we were pretty gratified at the ten, or the 16 letters of intent that we received in the end, the 10 applications because there were a lot of demands. I mean one had to rush out and, and, and find stakeholders that would be willing to co-fund in a matter of, you know, maybe four or five months. So. So that was, that was tough. One had to get a good proposal together. I think some really did opt not to not to apply.

Another thing to be said, Bob, is that we
also have kind of a different line of funding called the learning health systems funding four PPRNs and there are four PPRNs involved in this. I don't believe there's much overlap between the four that are in that. And you know, this is add on funding to the infrastructure funding.

Having said all that as the People Centered Research Foundation takes over managing the infrastructure. There will be an examination of the role of both CDRNs in PPRNs and it's not entirely clear that all 20, in fact, two of them have opted not to go forward in the next round. The PPRNs have been a challenge to work a work into this. And I think, you know, we were very gratified that four of them kind of proved the concept that they can and just suggest that others could follow their model. And in due course, find a partner, find a research question and come back to PCORI proper or go elsewhere.

CHAIRMAN NORQUIST: Okay. Any other questions about these grants that’s been were proposed? Allen or Harlin?
DR. DOUMA: No.

DR. KUMHOLZ: No, no questions.

CHAIRMAN NORQUIST: I need a motion to approve it. All right. So, let's see. Ellen you can be the second. Okay. All right. So Ellen will be the one who moved it and we’ll let Mike be the second. Okay. There we go. So all those in favor raise your hand and anybody opposed and abstaining?

On the phone, Allen?

DR. DOUMA: Aye.

CHAIRMAN NORQUIST: Harlan?

DR. KRUMHOLZ: Aye.

CHAIRMAN NORQUIST: Okay. So we're going to move back to where we were on the PCORnet update, but we need to skip down because I understand Dr. Masala you have to leave soon. So we'll let you go first. Okay.

DR. MARSALO: Thank you.

CHAIRMAN NORQUIST: I think he was going to have you go up there. Joe was going to sit over here and go up there, if you all go up there, all of you can just go up there and just kind of --
DR. SELBY: It’s my pleasure to introduce --

CHAIRMAN NORQUIST: I mean, if you want to sit here, it’s okay too, but -- all right. Adrian just go on up. Go on up.

DR. SELBY: It’s my pleasure to introduce Dr. Keith Marsolo and he has got to leave in 25 minutes, but Keith is the chair of the Data Committee of PCORnet and from Cincinnati Children’s Hospital, as you see, really been a real pillar and mainstay of PCORnet particularly around the common data model and the data efforts. Thanks for being here, Keith.

DR. MARSOLO: Sure, no problem. And I apologize for having to call an audible on the slides, but I appreciate it.

So, just to, I guess, reorient everybody as to why at least this part of the presentation is on today, so, at a previous board meeting there was essentially a request on the possibility of a searchable tool in the public domain to inform study feasibility and provide information on the conditions of interest.
And so, this presentation is essentially background on PCORnet’s current capabilities and some, essentially, potential options for the future. So, just wanted to talk about what we’re doing today and then what we might be able to do going forward.

So, when we talk about PCORnet and creating a PCORnet, our data strategy is to first standardize data to accommodate a model, then there’s a whole lot of work that goes into understanding the quality of the data through a process we call data curation, and then when it comes to actually running the queries, we operate a distributed query infrastructure where we have reusable parameterized tools that we use to query the data and essentially what goes to the partners is the question and then what comes back are the aggregate results and the summary statistics and that allows us to operate and ensure patient privacy and things like that.

And we have an iterative cycle of learning and improvement and the sort of infographic that we have around PCORnet, essentially there’s a front door, the requestor comes with a question that gets
turned into a query, the query gets sent to the network, they run the query, look at the results, send those back to the coordinating center, they get aggregated, and then returned to the requestor.

So, the tools that we have, essentially, the way that you can think about it, essentially, there's a type of question you might want to ask many times is we have the question, the study design, it then becomes parameterized where you can essentially substitute, you know, for diagnoses or age ranges or things like that, and it allows us to rapidly iterate to our queries.

The three main tools that we have for running queries within PCORnet, essentially they go really from simple to complex. So, the simplest is a menu-driven query, which is essentially a point and click interface that can be used to define cohorts based on things in the common data model, output can be stratified by things like age group, sex, race, ethnicity, and then we have the more complex PCORnet Modular Programs, or PMPs, that we use to assess more information, things like rates,
those are probably a little more kind of configure and deploy, and even further we can do these Cohort Quality Assessments, or CQAs, that we can use to identify the quality of data within a given cohort. And so, as an example of a menu-driven query, this was a fairly complex query that came through the front door looking at heart failure with preserved injection fractions. Essentially within a couple of days, we were able to turn the question into a query, distribute it to the partners, we give the partners a certain amount of time to respond, this case it was five days, and then a day to compile the report, so we were able to turn the query from a question to a report in eight business days, and you can see sort of a blown out subset of what was included in that, but it was things like -- we had co-morbidities, procedures, medications, and this is an example of the medication usage within that cohort.

So, that was essentially what -- like a whirlwind tour through the current capabilities of PCORnet, and so when we talk about the technical
infrastructure that we’ve set up, it’s really been driven by a series of governance decisions, so these were conscious decisions that the network made when we were getting started, so things like the queries would be distributed by the coordinating center, network partners or sites within the network can decide to run the queries and to return the results, and then partners would have a standard window to return results.

And so in this case it was ten business days, and the example I showed previously, that was five, because it was a rush, but the standard is ten business days.

And so, the infrastructure that we’ve created is really designed to support those governance decisions. And so, when we talk about potential options for the future, we have the opportunity of revisiting that governance and thinking about some different approaches. And the ones that I’m going to step through quickly, one example would be the development of a five or ten percent sample database, querying of some of our
data curation or data quality results, and then more rapid turnaround of simple queries.

So, when we talk about an X percent sample database, you know, the idea here would be partners would create a de-identified or anonymized subset of the common data model for a certain percentage of their population that would be submitted to a centralized repository that could then be used -- we could put the query on top of that.

And the benefits of this, is this is a real-time -- would allow real-time response and it could, in theory, allow public access. I think there’s a few drawbacks here, so one from the partners contributing the data side, there would be concerns about the misuse of the data, in particular the risk of re-identification, loss of confidentiality, and in terms of -- you know, that may require some risk mitigation on behalf of the CRF or PCORI.

The cost to develop and validate the methods for sampling and de-identification, this is non-trivial, and it’s likely that partners would
require their own subsequent validations to ensure that it’s working correctly, and then the development and hosting costs of this new query tool also have to be taken into account.

And I think one of the things to note about this opportunity in particular is that the new common rule changes some of the regulations around the reuse of EHR data for research, and depending on how that gets interpreted by IRBs going forward, this option may actually become a little bit more tractable than it would be today.

So, when we talk about sort of option two of querying our data curation results or our data quality results, so the coordinating center, every time the partners refresh their data, they send back a set of data curation results which are in the forms of aggregate -- hundreds of aggregate or univariate statistics that can be used to describe the content of the common data model. And so, we can certainly think about sharing these data more broadly to be used to answer simple questions about what’s in the data, what kind of population may
exist, and give a basic overview of the aggregate PCORnet population.

And so, the benefits of this approach is it’s a relatively low cost, low implementation burden solution. The data already exists. People are already running these queries. And then since the data exists as aggregate statistics, that helps mitigate some of the partner concerns that exist around re-identification. And, again, it’s real-time access to the information. The refresh is not in real-time, so there’s some delay in terms of the latency of this information, but access can certainly be real-time.

I think the big drawback to this approach is simply that the data curation results as they currently exist are only for single criteria or single variable queries, so number of females, number of patients with diabetes, not number of female patients with diabetes.

Now, we can also look at creating some additional canned reports on specific topics or populations that could be made available to provide
greater insight.

And then, finally, when we talk about option, three, which is really more rapid turnaround of simple queries -- so, the menu-driven query example that I showed with heart failure, you know, we can take some steps to increase through put through the network. So, one change would be we could certainly allow additional authorized users to generate and submit menu-driven queries beyond those people in the coordinating center. We can modify the process so the simple queries auto exits you and the results get returned without review instead of allowing, you know, partners a certain number of days to review the results and send them back, that can just happen automatically.

The benefits to this is it reuses the existing infrastructure, our query response time, instead of days, it’s sort of seconds, minutes, or hours, and this is similar to established approaches in other existing networks like Trinetics or the Accrual Clinical Trials, or ACT Network.

Sort of the drawbacks, there’s some changes
to the existing governance policies, so I mentioned sort of how governance works today, that would need to be changed, and then some additional costs to modify network infrastructure, to modify the status as things become more real-time in terms of a network, it just requires more monitoring to make sure that the systems are always up, and then there’s some additional technical support costs for having to manage and to train users.

So, just to sort of summarize, you know, option one, the X-percent sample, is really the solution that’s kind of closest to what you would consider to be a searchable tool in the public domain. However, the development costs to that area really non-trivial and there’s going to be some serious concerns about partners for the reuse of the data.

Option two, in terms of querying the data quality results, while limited, it does actually provide some insight into the data behind PCORnet, so if there’s a concern around, you know, how do we advertise sort of what’s there, this starts to pull
back the curtain and provide insights into what’s in the network.

And then option three, tracks activities in networks like ACT and then you can even take it a step further in terms of allowing other authorized users to query the network. If you start to open the door to funders or industry among those users, that starts to look like the Trinetics model.

All options are going to increase the overall infrastructure cost for PCORnet and we believe that option two is going to be probably the lowest cost, but I think one of our takeaways of this is just it’s important to figure out the sort of the external demand and how the selection of these different options might affect the marketability of PCORnet.

And then the last thing that I’d mention before I close is really these choices are not mutually exclusive, so we could certainly implement one, you know, the low cost option two, if we thought that was the best route, and then decide among the others at a later date.
CHAIRMAN NORQUIST: So, let’s open it for questions now, is that all right? Okay, so Barbra?

DR. McNEIL: [Off microphone.] A couple of questions. I’m a little confused. I thought the infrastructure that PCORI was providing to PCORnet actually took care of the costs of providing sample sized data, and yet you seem to indicate that the development costs for doing this are non-trivial. That’s question number one.

And question number two I didn’t understand is that the concerns about the partners about reuse of data -- it’s my understanding, CMS has a longstanding way of dealing with this that any time you get a sample size of, say, less than five, then you just don’t provide those data. If it’s greater than five -- or whatever the number is -- if it’s greater than that, there’s no chance that there could be any patient identification. So, maybe you could talk about both of those.

DR. MARSOLO: Sure. So, the way that the network operates today is essentially that the partners are funded to create essentially a full
population CBM that sits local at their institution. So, there’s efforts that they go to to essentially extract data from the EHR into the common data model, that sits locally, and then is used to respond to queries.

So, there’s not a sense of a sampling algorithm that says of the population that you have in the EHR, you’re going to pull five percent or ten percent, from that data set -- if that makes sense. And so the full population of every institution, every institution’s EHR, is in the common data model, and when we submit queries, the queries run against that full population.

DR. McNEIL: So, I don’t -- I guess maybe I’m dense because I haven’t had enough iced tea, so, what’s the extra cost there? I don’t understand that.

DR. MARSOLO: So, the cost would be -- so, if you were to say -- and in most places that exists as a limited data set, right, so that’s a data set that has dates and has identifiers in it, and the queries come and then what goes back are aggregate
results and summary statistics.

So, when you start talking about, can I take a slice of that dataset and ship it to PCORI, or some other third party, to sit and be aggregated for future queries as yet undefined, that starts to make the partners nervous because it’s different when the data sit behind their firewall and they can look at the queries that come in and then look at the queries that go back out and make sure that it sort of is doing what they want.

Once it goes outside of their walls, in some senses they lose control. I mean, there’s things you can do to make -- have PCORI or whoever’s holding the data sort of be the one that’s responsible for that and then they hold the risk if something goes wrong, but it’s generally -- it’s very different if you’re -- if the query comes in and I can understand the questions being asked as opposed to I’m providing data and then I have to essentially trust. That’s where, when you want to talk about then a dataset where you’re going to do sampling, it’s a question of, you know, how are you
doing the sampling, what are the fields that would
then be included in that extract, and it’s
essentially the cost of developing that is not zero
is basically it.

DR. McNEIL: So, I don’t want to drag this
on, but I think it might be useful to have a
separate discussion about this when you have more
time, because I know you’re running out, because it
strikes me that this is not so different than what
CMS does with Medicare data and what the ResDAC does
with data that they present, and I’m a little
confused about why this would be different?

CHAIRMAN NORQUIST: Adrian, do you --

DR. HERNANDEZ: Yeah, so like using a five
percent sample for CMS, so that goes through
extensive processing before getting to a five
percent sample that could actually be used in a more
public way. It’s only to be purchased, but again it
goes through processing that’s different than, say,
what institutions can do in terms of purchasing a
sample for a specific cohort for which they have
greater access to, say, PHI, so that’s the contrast
between the two.

The second thing, like as an example, it’s like for say clinical trials that say we’re running for NIH, when we’re putting together a dataset that can be deposited publicly, there’s extensive annotation so it can be used by anyone and also extensive processing so it can be used by anyone as opposed to, say, the raw dataset that’s used for analytical purposes.

DR. McNEIL: Maybe I just could repeat my request, Joe, I really think it would be nice to have a more detailed discussion about this because I still don’t get it and I actually do know a lot about data and Medicare data and this is just escaping me.

CHAIRMAN NORQUIST: Wait, wait, wait, why don’t we do that. But you had a second question too.

DR. McNEIL: No, the second question was --

CHAIRMAN NORQUIST: I want to be sure that before you run out --

DR. McNEIL: The second question was the
concern about the cost. And the second was about
the reuse when the sample sizes can be easily
defined as don’t do anything if they’re less than X,
then there can be no chance of re-identification,
but I think these are probably worth a much longer
discussion with sort of a systematic review of
everything and not have to rush through them now.

DR. SELBY: I think that’s a good idea,
Barbara. One thing to be said is that, unlike CMS,
which has been being asked for data for decades and
has finally gotten around to figuring out ways to
share it, these are healthcare delivery systems whom
-- some of whom just are participating in network
kinds of research with EHR data for the first time,
so they are a naïve, young, green group of
institutions compared to a CMS-like institution, and
you can’t just -- and they have extraordinary
concerns about the proprietary privacy as well as
the individual patient privacies.

DR. MARSOLO: Yeah, and I just think, in
closing, again, it’s not to say that it’s not
possible, I think it’s just to say that it’s not
free, and I think it’s going to take some thought to sort of develop the procedures and everything else that’s going to be needed to execute it.

MS. TROEGER: Well, I certainly support -- thank you for your presentation and I support what Barbara said about this requiring a little more time and just the ability to work through this thoughtfully.

As someone who’s been a tremendous proponent of let’s get in and see what PCORnet can do quickly to return results out to others, I’m probably closer to option two or option three, but I share your concern or the thought that if you are exporting datasets versus keeping things behind a firewall, behind a clean room within the CDRN itself, then it could just be queries -- how many diabetics in your population are on sulfonamides versus this or that.

Things very simple like three string queries, and I saw that some of them seem to be limited to one, you could find out how many were women, but not how many women were on Metformin or
1 something, in a population. I don’t know that that 
2 would be useful, but somewhere so that the integrity 
3 of the data sits within versus an export one 
4 percent, five percent, twelve percent where you’ve 
5 got the HIPAA concerns and everything else, shipping 
6 out would be something I’d like to explore. 
7 Similarly, how it complements versus competes with 
8 the CMS versus the AHRQ inpatient of the HCUP 
9 datasets and some of the other pieces so that the 
10 power of PCORnet can be accessed, and Alicia, I 
11 think you’ve spoken really eloquently in the past 
12 about the California sample that allows you to get 
13 in, do some quick stuff, and get an idea, can I do a 
14 study within this network looking at this 
15 population. 
16
17 DR. ZWOLAK: So, I also appreciate this 
18 great presentation and would amplify the previous 
19 questions, but also, I guess, the question for me 
20 is, is your report today informational only or are 
21 you expecting some advice or informed response from 
22 us, and if the latter, it seems to me that some 
23 information would be required about how much the
incremental expense is for these options.

DR. MARSOLO: Yeah, I think at this point it was mainly informational in response to the previous query. I think, again, as we look towards PCORnet and the transition, all of these options -- any of these options increase essentially the operating costs of the network and I think as we try to figure out how to make the network be the best steward of its money, think that’s where we would want to figure out which of these options is going to help the marketability of PCORnet and the sustainability of PCORnet going forward and we would sort of want to make a decision in that area.

SPEAKER: Just to take a step up, what you’ve been able to do, the kind of queries you’ve been able to run, the megasize of the data and the way you’ve been able to develop this common data model across literally tens of millions of people, it’s really downright amazing, and I think that’s something that we need to keep in mind while we’re -- this is a lovely problem to have, to think about, you know, which of these options we’re going to use
to query data -- high quality data on 80 million --
I’m probably underestimating -- however many
millions of people you’ve got, it’s -- I think
that’s important to keep in mind.

DR. SELBY: So, I think that when the Board
first raised this, we were seeing -- and Barbara,
correct me if I’m wrong, or Kathleen -- I think we
were seeing it as a real asset that would actually
enhance the familiarity of, for example, funders or
researchers with PCORnet, and actually drive
increased utilization. I think that’s actually a
point that we probably could use a little data on
and some more discussion between the Board, and I
don’t think I succeeded in making that case when I
took the notion to them, and so Keith is giving you,
well, this would cost money response, and it would
cost some.

I think part of the Board’s thinking was
that it would make money too --

MS. TROEGE: That there would be a
willingness to pay.

DR. SELBY: Yep.
MS. TROEGER: So, with a willingness to pay for the data --

DR. SELBY: Yeah, so --

MS. TROEGER: -- came some of the support. I mean, licenses to some of these more privately held more SQUARE datasets and IBM Watsons are tremendously expensive, so if there was a way to poll this, I think that was -- people might do rather quickly and inexpensively.

DR. SELBY: Barbara’s suggestion is --

DR. McNEIL: I think we definitely need more information. I think the devil is in the details here, and there are lots of data, and even though I understand data, I really would benefit a lot more from having a lot more information, so to systematically put down an understanding, what’s at the local site, what gets aggregated, what does it cost locally, what costs are consumed when the data are aggregated, what the concerns are locally, what the concerns are in an aggregated fashion, who has access to these data, for what cost, under what circumstances.
At this point, it’s probably a wonderful resource, but it’s too opaque for me to appreciate that.

DR. SIGAL: I just want to say, being very familiar with IMEDS and the central database and what we have done at FDA, I mean, we have spent over $25 million, maybe $30 million just on methodology. Now we have a user model that is being used by companies, and it’s expensive, it’s way more expensive than we thought it was going to be. And, you know, we have Harvard Children, we have the network, and to do these sophisticated studies, and I don’t know whether it’s the same or not, but I can tell you, it’s -- this is not trivial at all.

So, good work, and lots of stuff that needs to get done, but I know the complexity of this.

DR. FERNANDEZ: Thank you. I’m wondering what sort of information we need in order to have a more considered discussion, particularly around option one. And I’m wondering how we can get that information, because I don’t think it’s -- I think Barbara just outlined a whole series of excellent
questions, some of which need to be answered before we have that information, some of which can wait. And I’m wondering whether it would make sense to actually contract with someone to see what -- not only what it would cost, but what it would look like, what the timeframe would be, what the big decision points would be, so on and so forth, in order to get to option one, because I suspect it would not be an easy question for you all to be able to answer without making -- without it taking a good deal of your time.

So, in the interest of that, someday we’re going to want to get to option one, what does that look like?

SPEAKER: I think that there are two things with option one that -- just following on Alicia -- you know, one is how much it actually will cost, and it will cost a lot, and I think that the second item is the one that’s really more concerning, which doesn’t have to do with cost, but it has to do with the fact that as, Adrian, I think you said, or PJ, maybe you said it, that once the data leave the
firewall, then that creates a whole new set of very serious anxieties.

Then I think another part of this, if I understand this right, is that, maybe more for option three, because you say there are funders in the industry, that the idea of option three is that it not only provides useful information and answers queries, but I begins a conversation which could then lead to more research down the line, right?

DR. MARSOLO: Right, and I mean, fundamentally from a PCORnet perspective, I think in some senses you want to have the self service tool to be somewhat limited because what you really want is somebody to come to the front door and start having a conversation about a study that they want to run through the network, and that’s sort of -- that’s one part.

The other part is just that the data are so complex that it’s likely that they’re going to get sort of the wrong answer from the question that they ask and interpret it incorrectly, so that’s sort of the challenge with any self service tool on data.
that are these complex.

And so, I think, you know, trying to
balance those two issues with, again, really what
you want is somebody to pick up the phone and say,
hey, I’m thinking about this kind of study, does the
data exist, and then, how would I go about executing
that, which is what we’re doing today with the front
doors, putting queries to the network and trying to
turn those into studies.

DR. FERNANDEZ: I don’t think that there’s
any doubt that these are hugely important issues,
and on one level we absolutely want to encourage
people to come into the front door for the
sustainability. On another point of view, we have
spent a lot of public money on this and we want to
encourage research and a low barrier to entry. So,
I think these are exactly the sort of conversations,
including, for example, some of the technological
issues or advances that could come into play that
would mitigate peoples’ risks for loss of
confidentiality, these are exactly the sorts of
conversations that we need to be having.
So, it’s not a simple thing and I’m just not sure how we’re going to have that conversation without some really thoughtful pre-work being done. And I put that to the rest of the board in terms of what sort of information will we need in order to be able to have that as an informed conversation?

DR. SELBY: I think, Alicia, one way would be for us -- I should say that, Jesse -- Jesse Hudson is here, executive director or CEO of VCRF, Adrian is here, Keith is here -- we could have a follow up discussion now that the executive committee has heard the -- kind of the breadth of the board’s interest in this question.

You’ve done a better job than I was able to do of conveying what your thoughts were. We could come back to you with at least a proposal for how to discuss it further.

DR. FERNANDEZ: Don’t worry. People will always want to buy the data. I mean, researchers will want to buy the data.

SPEAKER: That’s kind of one of the things that also, I think, is probably harder to appreciate
is, is how do we use this to fit unmet needs of researchers compared to what’s out there, say, for example when you use a five percent Medicare sample, there’s something that are complete outcomes that everyone knows about. So, here we’re dealing with healthcare systems, which has variability in terms of complete outcome.

So, different sets of questions and then ultimately as we’re thinking about PCORnet, what are we aiming to do, which is to get to answers that have high impact, and so --

CHAIRMAN NORQUIST: Keith, do you need to go? Okay, I’ll depend on you to get up when you have to go. Just leave. It won’t be -- all right, so, Barb.

DR. FERNANDEZ: So, Joe, when you’re laying out the questions, as Alicia just mentioned, I think it would be very useful for -- I mentioned the five percent Medicare sample only because that’s what all the researchers in this room use the most, but there are other datasets that are not Medicare-specific, like TruVim and Optum and others, and it would be
useful to have it laid out exactly what you’re
giving versus what they are giving, for what price,
and with what level of completeness. Because
they’re -- well, period.

CHAIRMAN NORQUIST: Other questions or
comments to Dr. Marcelo before he leaves?

Okay, on the phone we have Harlan Krumholtz
and Allen Dumas. Did you have any questions now?

DR. KRUMHOLZ: None for me.

CHAIRMAN NORQUIST: Okay. All right.

Thanks, very much. I know you’ve got to get back.

And then we’ll let Adrian go. Okay, Adrian.

DR. HERNANDEZ: Okay. So, thanks everyone.

So, I’m here to give an update on Adaptable, one of
the key demonstration programs for PCORnet, and it’s
our large, pragmatic clinical trial. And so, here
we’re focusing on what has been the progress to date
in terms of the Adaptable model for identifying
potential participants and recruitment, and where we
think we stand there.

So, just as a reminder, Adaptable’s
answering the aspirin dose question, so what’s the
right dose of aspirin for preventing MIs and other cardiovascular events versus the safety issue of bleeding. The aim is to randomize 15,000 participants. We aim to identify all those through PCORnet and then leveraging PCORnet after their enrolled, be able to have a follow up for the clinical events via PCORnet as well as a linkage to other data sources such as Medicare data.

In terms of recruitment, one of the things that when we started Adaptable is that -- what I call a very ultra pragmatic trial, we did not know which way would be on the best recruitment method. We actually had different networks approaching recruitment in different ways, and then also more recently, a health plan joined and that’s been recruiting potential participants directly through their beneficiary list.

And so, there are kind of two buckets here, one is low touch, another is, so called high touch, and so low touch is we’re essentially doing things electronically, so electronic health record best practice alerts, emails to potential participants as
Well as snail mail, and then towards a higher touch, things that happen through the clinical flow, so, people they’re identifying as they come through the clinic and then having direct discussions about Adaptable in clinic on tablets or people are using them while they’re waiting for their appointments as well as direct phone calls for participants here. And for the most part, we’ve found that a multi-touch approach using a combination of these efforts actually was the best.

The other thing we learned along the way was when we designed Adaptable for the inclusion/exclusion criteria we thought we had very broad criteria that was used, but the thing we learned was that there’s some criteria that didn’t translate easily to how people actually think about clinical care and electronic health records.

And so, for example, in one key enrichment criteria was having people who had heart flare low ejection fraction less than 50 percent, the on thing that comes up is that’s not often coded in a structured way, but rather we find things in terms
of chronic, systolic, or diastolic heart flare, or things like that. Another thing was in terms of blood pressure measurements, again, if you were to just use hypertension, actually, we have access to direct blood pressure measurements, and so what is that that’s being used.

And so, we actually went through a protocol amendment after seeing how our computable phenotype worked, and then revisiting it when we looked to see how to maximize or optimize the study by the experience with PCORnet and then went through an amendment that increased our potential participant pool without changing the scientific objectives.

And so, this kind of learning with improving the computable phenotype and enrollment has been helpful in terms of optimizing the electronic eligibility criteria with what is really available routinely in EHR data, and then also being able to understand the sensitivity and specificity around that, and also dealing with variability across data marks also allowed us to help, as we went forward, to kind of test different approaches
as we went through what’s the different types of criteria, so we can make sure we didn’t lose sensitivity or specificity that were undesirable, and then also, we went through some other things that included a review of implement of local filters that they were in place that limited, in terms of what the potential pool for actually unnecessary reasons.

So, we discovered that after the fact that someone said, well, I don’t want X-type of patients to be approached because of my own clinical practice, which when that wasn’t really evidence-based or actually relevant to the whole practice, and so there are things like that. And like, examples where they were thinking about potential participants for, say, a device trial, and so they wanted to make sure that they weren’t approached.

Another thing is refreshing, in a more frequent way, so that we can identify those who are newly eligible patients start walking through that health system.

So, just to give you a sense of how this
works, so, like, the centers supply the computable phenotype, they generate a list of potential eligible participants. They get what’s called a Golden Ticket, so, like your ticket into the trial, and that’s why it’s called a Golden Ticket, then when they have either been reached electronically or through a letter, then they can enter that code to join a study or, really, just to learn about it, and so you could actually go onto adaptablepatient.com to actually explore this and hit the “No Code, No Problem” approach, but ultimately you need to have a code, so that we can actually link you back into a health system to have your complete follow up.

Then when you go through this, and you can go through the five steps to joining the study, you can also share this information with other members of your family, your clinician, you can go back to it later, and all this was designed with our team of adaptors, our patient partners here for Adaptable.

To give you a sense of what a typical center does, where they have a phased recruitment strategy of approaching 200 to 500 patients per
week. They will have an email that will go to a

group of potential participants. They will have

some that accept it. Those who decline, they will

remove them out from the list. Those who don’t

accept, they’ll have a follow up phone call visit to

answer any questions, and then they kind of cycle

through this until they get a couple touches through

e-contact as well as by phone to see if they have

any information -- any questions about the

information provided, then also be able to join the

study and facilitate that across the study. And so

this has been a coordinated and helpful example

across PCORnet.

To give you a sense of kind of different

methods that have worked, so we’ve tested a variety

of methods, these are the most common ones. There

have also been some uncommon ones including reaching

out to local churches and largely -- you can see

here in the box -- what we call the conversion rate,

if they touch the portal in some way, what’s the

percent that will actually ultimately enroll, and so

the so-called in clinic tablet, of course, has the
highest rate, but it’s also the most intensive. E-
communication or letter is reasonable at 38 and 40
percent, and telephone is 50 percent. But again,
this is after people actually go and click on the
Golden Ticket.

This is where we stand as of when these
slides were put together. So, there are 33 sites
that are actually actively enrolling out of 37 that
are active. Almost 300,000 have been approached.
Actually, as of today, we’ve enrolled just over
8,100 participants in Adaptable, and last week, to
give you an example, we enrolled 134.

And as things have progressed, we’ve
definitely been learning, so when we first started
the study in April 2016, we had two sites enrolled,
eight participants for the month out of 126, and
then a year later we were enrolling 600 for the
month of April at 26 sites, and had kind of
maintained average enrollment around 400 to 500 for
the remainder of that time out of 32 sites.

And then the other thing is along the way,
in November was a large reach out by one of the
health plans, Health Corps, which reached out to over 100,000 of potential participants.

One aspect that we’re now very attentive -- have been as well at the beginning, is it’s not just about recruitment and participating in Adaptable, but also how people stay in the study so that we can get a high quality answer, and early on there was some variation regarding withdraw of consent for participation, and so that caused us to help modify what’s the enrollment criteria, who we’re approaching, and also having early contact for anyone who seemed at risk for withdrawal, and that has been decreasing over time.

But you can see here across the ten different networks, there’s variation in terms of percent, withdrawal of consent, which is overall about 1.7 percent, but we also have gotten permission from some of those who actually have passive follow up, which is actually very helpful. One of the concerns that has come up for the reasons why is medication or health issues, something changed, and so they didn’t understand why they
should continue to participate, and then privacy concerns has come up.

We’ll have to see if that increases in any way because of a public attention to privacy that currently exists.

So, what are the key lessons that we learned from Adaptable, one is kind of a group of kind of what we call successes, it’s been tremendously fun working with Adaptors, our patient partners across the nation, they’ve been one of, I guess, champions for the study, kept us pretty honest about things, and they’ve been ambassadors for a variety of national meetings and also through our engagement with other organizations.

The national societies have been very positive about partnering here. The ability to identify hundreds of thousands of people who are eligible and being able to approach them is considered a success. This is where we say, you know, data is necessary, but it’s not sufficient. How you actually reach them is really important.

There are challenges here, and so one is,
you know, we have seen varied recruitment across the centers. Partly, we think that’s the variation in terms of clinical and patient engagement across the centers and sites. Those who have really a local strong “leadership and engagement”, they seem to be more successful.

There’s also been different areas where there’s lack of integration in the clinical and the trial personnel and informatics teams as to how to bring those groups together for team science.

We’ve also discovered a variety of institutional policies and procedures and barriers that some places are over ten years old, and the way I kind of describe that is about -- just over ten years ago, the iPhone was invented, so there are things that change in the world, but their policies have not changed, and so like they will still require things to be sent by mail to let you know that we’re going to email you.

And so, I think along the way we are going to have groups -- writing groups around these different challenges to note what needs to be
changed with the system.

And then in terms of as we go forward, in terms of future, we certainly see how to kind of continue on some of the things that have been developed from Adaptable.

We see areas for future studies in terms of improving engagement, specifically testing different engagement models. We did some in here, but like there’s certainly more to do in terms of the science of engagement. Also understanding patient preferences for research, so being more proactive about who wants to participate in research, what type of research, a variety of other approaches in terms of engaging and approaching people for participation.

And then the other thing that we’re starting to think more and more about is how do we actually return value to participants? So, the ultimate way to enhance recruitment and retention is to have a deep commitment that at the beginning, that like we are committed to doing five things and so that way you know as long as you go with us, we
are committed to returning there.

   We have that for Adaptable, but I think now in retrospect, I think we could have done an even better job of saying, this is going to be our commitment for you as you join, and that would be something that we would endorse for future studies.

   And then the other thing is using Adaptable to change institutional policies, how things vary across different centers for really local reasons that are not necessarily so-called evidence-based, and then being able to prioritize PCORnet because of the values it brings in terms of the impact.

   So, I’ll stop there and answer any questions.

   CHAIRMAN NORQUIST: So let’s open it -- Bob Zwolak.

   DR. ZWOLAK: So, I’m sure we all really appreciate this update and it may be that the lessons learned here are inestimably important. The question I had involves the actual goal of the research study. We had in 2015 and 2016, the target was 20,000 registrants and in an application for
incremental funding in 2016 it was stated that 14,000 would not be enough, would be underpowered, and now 15,000 is the goal.

So, in addition to all these fabulous lessons, is there a likelihood -- is there still a good likelihood of a meaningfully important result to this test of the right aspirin dose?

DR. HERNANDEZ: Yeah, so I guess one of the things that comes up is we had assumptions when we were putting together Adaptable, and a range of assumptions, actually, in our application for Adaptable in terms of the power that was needed to answer what’s the difference between 81 and 325, so 20,000 essentially was giving us around 90 percent power and recognizing where things were going in terms of recruitment rates relative to what we would want for having the answer within a reasonable time period. We felt that it was appropriate to have -- finish the study within a reasonable time period going at 15,000, so that gives us about approximately 85 percent power, so that’s kind of the trade off. So, it’s essentially time versus
DR. FERNANDEZ: That was a fabulous, terrific presentation and it’s so good to see this. So, here’s a quick question, which is, I see that e-identification and the e-approach works and it’s still the modal way in which you’re getting people in, right, and that’s really important.

On the other hand, there’s going to be few studies, maybe no studies, that is as easy and as straight forward as Adaptable in terms of what’s being tested.

So, my question has to do with the underlying conceptual model of PCORnet recruitment. And what are your thoughts, and could you give us some data at some point around is it possible to recruit from clinics if there is no clinical champion and if there are no incentives for the physician, because as I understand this model correctly, there are no physician incentives. And so, for the physician, it’s only altruism that offsets the loss to time and effort, or if there’s a clinical champion, then maybe you do it because, you
know, you want to keep Dr. [inaudible] happy, you
know, whatever.

So, what are your thoughts around this in
terms of that larger lesson? And at some point do
you think you could break down the clinical stuff
for us?

DR. HERNANDEZ: Yes, so incentives matter.

And so I think that’s where me saying that for
Adaptable, where it really matters is when there are
clinical champions and clinical leadership, because
they say this is going to be really important for
the population that we care for. So, there’s other
values that they’re bringing to the table.

I’ll say that the way I characterize
Adaptable is that the ultra pragmatic trial and
there are components of this that can be readily
used for other studies. So, for example, there are
maybe, say, a high interest area in diabetes where
there’s multiple agents that are being considered.

What would you do for doing this where you can
identify people, reach out to them, see if they’re
interested in participating? But they ultimately
would have to come in for a prescription or get a study drug.

But you can do things that can help focus who is actually potentially interested, as opposed to right now, which is just by chance. Passively someone happens to come to a clinic and the study coordinator happens to be there at the right time and the physician happens to remember that.

All that kind of luck is just not efficient and it’s not very effective. So, we think that you can take components of this to apply it in a variety of ways. And then for studies that are more pragmatic, say, one-time interventions, such as like a vaccine, then that would work well. For things that’s going to need something more intense in terms of either follow up or drug accountability and so forth, there are going to be some things that you have to do the traditional way.

The other thing is when we have data that’s recurring that’s in the background, that lessens the burden for participants, they don’t need to come in every four weeks for their study visit. They don’t
need to come in for some of the blood work, perhaps, that can be done at home.

DR. FERNANDEZ: I think there’s been this view that it was sort of magic --

DR. HERNANDEZ: I wish.

DR. FERNANDEZ: -- for recruitment and I think that what I think the Adaptable experience has done for me, and perhaps it’s done for others on the board, is that it’s disabused the magic of enrollment, and I guess this is something that I just want to make sure that we’re all hearing, which is how much work it’s been to enroll for a trial of aspirin.

And because I really don’t know how much, for example, this issue on second agent for diabetes, which would also require a huge sample size. But it’s not an easy question and patients will have to talk to their physicians about it, and I’m not seeing, in the PCORnet framing, I’m thinking that we still have a lot of lessons to learn about all the ways in which it can help us in recruitment, as you say, making sure the email goes at least to
the right people.

But it’s not so simple, and congratulations to you and the team for doing so well.

DR. HERNANDEZ: I agree, it’s definitely not magic. I mean, one thing is, as a cardiologist, certainly I think that aspirin is like terrifically interesting and I always get surprised when people, so like --

DR. FERNANDEZ: [Inaudible] -- over-the-counter drugs --

DR. HERNANDEZ: Right, right, no, but here’s my kind of personal story. I’ve got two parents, they’re eligible for Adaptable, they get approached. One signed up, easy. The other one had questions, didn’t think that she could talk to her son, who’s a cardiologist, who may know something, hasn’t talked to her cardiologist who is trusted and who is not myself, so I get, you know, that’s -- to me, like my personal two examples, one just said, I’ll sign up for it, and then the other one went through all this and she decides she wasn’t going to do it because she’s worried about bruising.
CHAIRMAN NORQUIST: Barbara and then Mike.

DR. McNEIL: I agree. I really like that presentation. I particularly like this last slide. But I have two questions. The first one is, as I understand it, you went through the medical records, circle various things, got a patient population, and then they got randomized to A versus B. So, the real question is, or a real question is, the extent to which these data are true and reliable depends upon the extent to which across all the various sites the population that was subsequently randomized is, A, the same across sites, and B, something that the cardiologists will buy into as a reasonable patient cohort for deciding whether it’s 81 or 300-something.

So, that would be the first question. And the second question is a little bit related, and now I’m way out of my field, is -- but it’s probably for you or Michael or Harlan, who’s not here, to say, to what extent is the power of 85 percent enough to make a decision between a low-dose and a high-dose aspirin when the stakes are reasonably high and when
there’s a long history of low-dose. So those are
the two questions. They’re easy, so just go for it.

DR. HERNANDEZ: Yeah, so for the first
question when we did a section for each site, partly
to get comfort with the clinicians, we asked them to
actually for the first 50 or so participants, to
actually review the charts. And so we actually have
that. That was something that we thought would be
important for people to get comfortable. So that’s
there, what we did and we have some other validation
work that we’re doing.

For the second question in terms of the
history of 81 versus 325 is that, you know, we --
there’s actually a variation in practice across
that, and so we actually -- you know, there’s
publications around that why everyone would say,
like -- and you see camps of people, they’ll say,
oh, no, it’s 325, oh, no, it’s 81, but practice
shows there’s variation. Actually, in the
guidelines it actually specifies -- one of the few
times in the cardiovascular guidelines it actually
specifies this is an unanswered question that
Adaptable will be filling in. So, that’s unusual to see.

CHAIRMAN NORQUIST: Mike?

DR. LAUER: So, congratulations. It’s just incredible, the progress that you’ve made. I think you’ve made a couple of important points.

One is, is that, in a way, this is an effort of systematizing enrollment to in systematizing interest in trials, and, as you say, you’re getting around the luck component and you’ve developed a system by which huge numbers of people are being contacted.

To get to Alicia’s question, one key point to enrollment is that you pick topics that both patients and doctors really care enormously about. You know, one trial that Adrian and I know very well was the trial of -- was the serotype this is a drug for heart failure. There was a huge amount of controversy about that and that trial enrolled very quickly and it’s because people really wanted to know the answer. I think aspirin is something that, when we were first discussing this a few years ago,
this is something that we really, really do want to know the answer. And so, I think that’s another critical part to this.

And then the third, which is probably going to be something that will happen over time, some institutions have started to do this where the top level executives say that the way they’re going to measure their executive’s performance is by how well they are getting patients enrolled in clinical trials. There have been some universities where this has actually happened. And it’s amazing what happens when an executive is told that the way you’re going to be measured is by how well you’re participating in this value of the institution, things start to change.

DR. HERNANDEZ: Yeah, so, actually, on a local level, we’re actually pushing for that as kind of a part of the balanced score card for leaders so that they recognize that part of the mission is to generate knowledge, and the you do that is actually participation, and so, again, that helps recognize that. Because I think, at least to your point,
there’s been so many other competing priorities, it’s really hard otherwise.

CHAIRMAN NORQUIST: Any questions on the phone? Allen or Harlan?

They must have dropped off or they’re muted and they can’t get on. Other questions, Adrian, do you have something else you wanted to say?

Thank you very much. I mean, it’s very helpful.

[Applause.]

CHAIRMAN NORQUIST: And we will follow up on -- I just want to say, because we’re coming up on the public comment period, that there will not be a public comment period today. We don’t have anyone who wanted to appear in person or on the phone. So, we always welcome feedback at info@pcori.org or through our website.

So, Joe?

DR. DOUMA: Joe, this is Allen.

CHAIRMAN NORQUIST: Allen, go ahead.

DR. DOUMA: I’m sorry, I was on mute. Any update on the process, the timeline for having a
more definitive business plan?

DR. SELBY: We -- that’s a good question for tomorrow on the RTC. I think Kathy Hudson will make some preliminary comments on plans for the business plan and then a month from now on the RTC, and shortly after that at the board, we will talk in more detail about the business plan, but thanks for asking. We all have it as a very high priority item for a number of reasons, not the least of which is you, Allen.

DR. DOUMA: Well, thank you.

DR. SELBY: Yes, thank you. Okay, so you heard Adrian mention score cards and in fact one of the other questions from the board in February was about a dashboard on PCORnet, and it’s gratifying because we’ve gotten used to dashboards ourselves with PCORI, and I will say that Duke is actually very good at developing dashboards and they’ve been using them internally for a while, but just use them to share among the networks in PCORnet and with the executive committee to follow dichotomous things like has the master DSA and the single IRB been...
signed off on yet, but also to monitor things over time, like query fulfillment and turnaround time rates.

So, we’re actually grateful for the question from the board and happy to come up with a dashboard that would be suitable for sharing on a quarterly basis with the PCORI board and I imagine it would probably give the PCRF board an appetite for this as well, as well as the public. But we do see them more at this point as longitudinal records of progress on measures that can improve over time.

So, I’m just going to go through some -- we had a nice discussion on the RTC last month, and just before we put the first dashboard together, I want to show you some metrics and give you a chance to comment on these or add other suggestions as well.

So, you can think about them in different buckets, so the number of patients who are in the network, the number who have had at least an encounter in the last 12 months, the number of patients who are available for -- and an encounter
in the last month, you might think that they’d be somewhat more reasonable to approach about a trial -- patients available for an observational study would be people who have had a certain amount of follow up but not necessarily an encounter lately.

So, I also realize it’s very late in the day and people are tired, but as we’re going through these, anything that occurs to you that I can take back to the coordinating center, I will be really happy to do it. But those are patient metrics.

Front door activities, the number of front door requests we’re receiving and how that’s changing over time, over all and by requestor type, was this a funder, was this an external researcher, was it a network researcher, and the number of requests. The number of funded research projects by federally funded, industry funded, number and award for both demonstration and competitive projects funded by PCORI. Kathleen?

MS. TROEGER: Joe just to contribute this in real-time, I would be interested in knowing if they are novel as well, so if there are three
requests, you, me and Larry, that’s interesting

versus me kind of coming back --

DR. SELBY: So, the number of novel
requesters, independent.

CHAIRMAN NORQUIST: Unique.

DR. SELBY: Unique. That’s the word we
were both looking for.

Okay, in terms of research and performance,
if we have a clinical trial, like Adaptable, or like
the invested trial or like some of these new PaCR
awards, the average days it takes to activate a
site, the average days to the first patient that’s
enrolled, the average enrollment time, total
enrollment, percent of the target enrolled,
population enrolled, and the number of trials with
data reported. So, this would be on a -- these are
calculated at the trial level, but they could also
be calculated, I guess, at the site level.

And then, of course, number of manuscripts
overall within studies. And then on queries, the
number of queries that have been executed to date,
the average query turnaround time, and the listing
of queries, which would come as an addendum to the dashboard by therapeutic area.

And then those last two, which I think are pretty much at 100 percent now, they’re very high, the percent signed on to the data sharing agreement and to the smart IRB agreement. Barbara?

DR. McNEIL: So, Joe, this looks awfully ambitious in terms of putting all these together in a dashboard and I wonder if you might -- or maybe everybody could digest all of this, but would it make sense to prioritize them and say for the first dashboard you’re going to have ten of these that are really robust? Because this is mind boggling that you could really get all these --

DR. SELBY: Yes. And this is really -- that’s the intent here. These are possibilities. You’re right. There won’t be nearly all of these and any comments you’d like to make about things that are more attractive/less attractive, would help us to prioritize what -- so, thank you. I probably didn’t say that clearly at the outset.

CHAIRMAN NORQUIST: I think Bob had a
question.

DR. SELBY: Yes, Bob.

DR. ZWOLAK: In the world of better, faster, cheaper, there’s a lot of faster on here, which I really like. It probably would be quite difficult to get it cheaper, but maybe not, the expense per enrollee or expense per completion, and better I wonder about patient-centric metrics of some sort.

DR. SELBY: Great thoughts. Kathleen, did you have another? Go for it.

MS. TROEGER: And maybe we want to consider pragmatic in here as well as its own category. So, just with all the work -- and Ellen’s not here -- that’s being done for real world, I’m just not sure we’re limiting ourselves to RCT’s and prospectives.

DR. SELBY: Okay, so when you say pragmatic, you mean pragmatic trials or did you have a different notion --

MS. TROEGER: Yeah, so I’m thinking about it in real-time here, Joe, I don’t have a strong proposal, but I would suggest that there may be --
that we want to ask how it fits and then count the
metrics, so maybe we just want another classifier at
the top for observational --

   DR. SELBY: Yes. And cluster -- RCT

clusters?

   MS. TROEGE: Yeah, same idea. I think

that’s it, and so if there are not other comments or
suggestions --

   DR. SELBY: So, I think that’s it, and so

if there are not other comments or suggestions.

   CHAIRMAN NORQUIST: So I think the only

ting I didn’t see, when you talked about the
population on the first slide, I don’t see anything
about the diversity of the population. Because, you
know, if it was of interest to note, you know, just
as you do more of that, what the diversity is of the
population that you’re enrolling.

   DR. SELBY: So, we will take this and mock

up an initial dashboard and try to have something
from each of these sectors and bring it back, and
you can have at it again. I think our experience is

that dashboards get better and better over time.
CHAIRMAN NORQUIST: Any other questions about that or comments? Yeah, as people think of things, obviously send them to Joe. But I agree with Barbara, you might want to prioritize a few just to get started.

Okay, Joe, do you have anything else?

DR. SELBY: No, Gray that’s it for today.

CHAIRMAN NORQUIST: Okay, so anything else for members of the board on the phone? Okay, so, I want to thank all who joined us today. A reminder, all the materials presented today will soon be available on our website. The webinar was recorded and will be archived probably by next week.

We always welcome your feedback at info@pcori.org or through our website. Thanks everybody.

[Whereupon, at 5:20 p.m., the meeting was adjourned.]