PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

BOARD OF GOVERNORS MEETING

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Washington, DC 20005

[Transcribed from PCORI teleconference.]

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Ellen Sigal, PhD
Harlan Weisman, MD [via telephone]
Robert Zwolak, MD, PhD

AGENDA

AGENDA [Continued]

AGENDA [Continued]

P R O C E E D I N G S

[10:01 a.m.]

OPERATOR: The conference is now being recorded. Dr. Norquist, the floor is yours.

DR. NORQUIST: Thanks. Hello. I'm Dr. Gray Norquist, Chair of the PCORI Board of Governors, and I want to welcome those of you who are joining us for today's Board meeting, which is being held in Washington, D.C., as well as via teleconference and webinar. Thank you to everyone who has registered to join us in person, online, or on the phone, and we are pleased to have you here.

As a reminder, instructions for logging in or calling in are available on our Web site at PCODRI.org/events.

All Board members are present in person except Allen Douma and Harlan Weisman, who are joining us on the phone.

I want to remind everyone that disclosures of conflicts of interest for members of the Board of Governors are publicly available on PCORI's Web site and are required to be updated annually.

Members of the Board of Governors are also 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 were to deliberate or take actions on a matter that presents a conflict of interest for you, please inform me so that we can discuss how to address the issue. If you have questions about conflict of interest disclosures or recusal, please contact your staff representative.

All materials presented to the Board for consideration today will be available during the webinar and then after will be posted on our Web site at PCORI.org.

The webinar is being recorded, and an archive will be posted within a day or so. We have scheduled public comment today from 5:15 to 5:45 Eastern Daylight Time. If you are interested in registering to provide public comment, please visit our Event page for instructions. You also can always email us at info@PCORI.org or provide input through out Web site at PCORI.org.

Finally, a reminder, we are live Tweeting today's activities on Twitter. You can join the conversation at #PCORI.

The first item is roll call. I think we can basically just announce we have all the members here present. Robin is here for the Methodology Committee. Allen, are you on the phone? Allen Douma?

Allen must not have joined yet. Harlan Weisman? Okay. When they come on, we will certainly announce it.

The first item on the agenda is our consent agenda. Those items are up there. One is the minutes from our recent April 26 teleconference, and then the nomination of Dr. Andrew Bindman to serve on the EDIC and SOC. We want to welcome Dr. Bindman who is now with us and at AHRQ. The updated research and infrastructure project budget increase policy.

We need to go to the point at which we ask for a motion, and then we can have a discussion. Don't we have a slide? There we go. I need a

motion to approve the consent agenda.

M O T I O N

MR. BECKER: So move.

MR. LIPSTEIN: Second.

DR. NORQUIST: Larry, thank you, and second from Steve, thank you. Now we can open it up for discussion. Let's first address the minutes. Are there any corrections or additions to the minutes?

[No response.]

DR. NORQUIST: Any concerns about Dr. Bindman? I don't think so.

[No response.]

DR. NORQUIST: Okay. Good, we're getting off to a good start. The last one is about the policy. Do we have any comments on the proposed policy? Larry, did you want to say anything, the policy on the change in the amounts?

MR. BECKER: It's an adjustment to our existing policy. I don't know that it necessarily warrants a whole lot of discussion. If there are questions, I'm sure we can respond to them.

DR. NORQUIST: I don't see any questions or

concerns. Wait. Leah?

MS. HOLE-MARSHALL: My question was it looked like there was both a supplemental with a max of $1 million or 5 percent, but then the general was a max of $1 million or 30 percent, up to 30 percent. I just wanted to understand the difference between those two, and since the old policy wasn't included, I wasn't sure what the extent of the change was.

Many of our grants are only around the 3 to $5 million, so $1 million is a pretty substantial number.

MS. YAN: Our previous policy adjusted for ops, so because now we have so much bigger awards, that is why we had to adjust the policy to reflect that.

MS. HOLE-MARSHALL: The previous policy was up to 15 percent?

MS. YAN: What happened is when the Board approved the slate, the amount is based on what they requested at the proposal. Usually, after review and budget negotiation, the amount is slightly different, so we put 15 percent there so it doesn't

have to come back to the Board.

That 15 percent has worked really well the last couple of years. We haven't had any problems. Now, with much bigger awards, we feel we need to have a more comprehensive, more complete policy in place to address all issues. That is why we made that adjustment.

MS. HOLE-MARSHALL: Maybe what we can do in the report out for either the Dashboard or how our grants are doing, if you could do a report about how many were adjusted and at what percent so we can continue to track that.

MS. YAN: Certainly. Currently, we prepare those reports for FAC as well.

MS. HOLE-MARSHALL: Thank you.

DR. NORQUIST: I think we can do this by voice vote. All those in favor?

[Chorus of ayes.]

DR. NORQUIST: Anyone opposed?

[No response.]

DR. NORQUIST: Anyone abstain?

[No response.]

DR. NORQUIST: Allen or Harlan Weisman, are you on the phone?

[No response.]

DR. NORQUIST: All right. The next item is our Executive Director's report. Joe Selby, of course, is our Executive Director and will deliver that report. Joe?

DR. SELBY: Thanks, Gray. Good morning, everyone. I'm concerned about the people who are not able to see Andy Bindman directly, so all those listening by webinar, here is a picture of Dr. Bindman. I just wanted to say how delighted personally I am and how excited we all are to have Andy as the new Director of AHRQ.

Andy is a primary care physician, health policy, health services researcher, head of General Internal Medicine at San Francisco General Hospital. Important for all of you to know formally, Alicia Fernandez's boss. That is why we recruited him here.

[Laughter.]

DR. SELBY: Andy is just a real force and a

delightful person. It really is great news for AHRQ and great news for PCORI to have him in the D.C. area and on our Board, and at the helm at AHRQ. Welcome, Andy.

I usually throw in a few nice brief stories here. This is one that is just really pretty dramatic. PCORI has been pushing the envelope on patient engagement in terms of getting research off the ground. THE BMJ has joined us, and not without acknowledging our role in the process -- have joined us in tying down that other end of science, that end that comes at publication.

The British Medical Journal has now launched an initiative that involves three things. Number one, if you submit a paper to the British Medical Journal, you have to state in the text of the paper whether and how you involve patients in developing and conducting the research.

Patients have been incorporated into the peer review process, so there is a patient reviewer and onto the editorial board of the BMJ. This is really -- you see the quote there that references

PCORI. We have had conversations with them and really are looking forward to working with them to understand the impact of patients at this tail end -- not the tail end perhaps, this particular branch in the project of producing and disseminating science. That is just a nice tale.

Many of you know, but it is important for the public to hear as well that at our March Board meeting we announced -- it wasn't a topic that needed Board approval, but the SOC announced that we would be releasing a funding announcement for a randomized placebo controlled trial of direct acting antivirals versus active surveillance in patients with Hepatitis C.

The focus was on short-term outcomes. The focus was on symptoms, such as fatigue, depression, mental cloudiness, ability to function. The idea was to see whether in fact the impression of clinicians and patients that treatment with direct acting antivirals actually affected these endpoints in a number of patients, that is low risk patients who don't have coverage for Hepatitis C treatment.

This was announced. We actually had presented a time line. Shortly after the Board meeting, we got communication from a number of patient stakeholder groups in particular, physicians as well, clinicians as well, and people who had participated in our original meeting in October 2014 saying this was not discussed in 2014, and we feel it needs more airing and more stakeholder input.

The Board decided to stop for the moment our process moving toward release of a funding announcement and reconvene this group. We did it last Thursday afternoon, a two hour plus teleconference/webinar, extraordinarily well attended. I think we had almost everybody who was at the first meeting rejoined us.

I would say the meeting reflected the complexity of this issue. There were a wide range of opinions presented on the scientific utility or value of the question, pro's and con's, on the ethics of the question, and on the feasibility of conducting a study in the present environment.

That input is being synthesized. We will

go back to the SOC, take that under advisement, and we will let the public know as soon as there is a decision based on the input from this stakeholder meeting.

I just wanted to get that on the public record since there may be people listening in who are wondering what has happened to that funding announcement.

I should have said that meeting was fully open to the public, and they were able to submit comments as well.

Annual meeting, good news is the date and time are set, November 17-19, National Harbor, here in the D.C. area. A full second year agenda that builds on what we accomplished with a very successful first annual meeting. The spotlight is going to be on the role PCORI can play in promoting CER and patient-centered outcomes research.

This year we are able to focus on emerging results of our funded studies. That is quite exciting, on building the community on emerging dissemination work and building the community to

effect dissemination and knowledge sharing.

Should be an exciting meeting, and I really hope as many Board members as can possibly attend do make it. As you know, there are roles we are soliciting in activities and contributions from you during the meeting.

This is the agenda for today's meeting. In just a second, I will present briefly the Dashboard for the second quarter. You're going to hear a mid-year, through the second quarter of fiscal year 2016 financial report from Regina and Larry of the FAC.

Robin Newhouse will present the Methodology Committee report. This will be a vote proposal from the Selection Committee. Rachael Fleurence will present on a cross-PPRN research project, a very exciting project that we will get all 20 PPRNs involved in research activity.

Then you are going to hear a report from Jean, Regina, and Evelyn on the application enhancement efforts, which are really the result of ongoing discussions and subcommittee work primarily coming out of the SOC and staff on efforts to

enhance every aspect of the application process and the application experience of researchers.

The message here is that Board and staff alike are listening to the research community, are listening to our merit review panels, and are working in a systematic way to continue to make improvements on the application process. You will hear about that.

Noontime, just after lunch, we will have a panel presentation. This month's stakeholder focus is on specialty physician organizations. We will hear from the American College of Physicians, the American Thoracic Society, and ASCO, the oncology specialty organization. We have had really fruitful relationships with a large number of physician specialty organizations.

In the afternoon you will hear a pretty lengthy, for the first time, a full presentation on PCORI's dissemination strategy. We are anxious to present this and have a discussion with you about this as we enter the phase of life where dissemination is really something we can talk about

and not only talk about, but carry out.

Then there are three exciting new funding announcements presented to you on behalf of the SOC for your consideration for approval, and if you approve them, we will develop and get these funding announcements out, on sickle cell disease, on prevention of unsafe opioid prescribing in primary care, and on community-based palliative care.

We are going to do a little catch up work with a couple awards that were delayed from previous cycles, delayed because of questions. The questions have been addressed. I think it is two or three additional awards.

Then an analysis presented by Evelyn from work in our portfolio on the outcomes of depression, pain, sleep, and fatigue. We have often heard from you that we should be conducting more studies with these as outcomes. This is one way to approach that, to present to you what we are currently funding in these areas, and to get a discussion about how we can build on this, synthesize your input, and questions will be welcome.

With that, there are just two more things I want to say in closing today. The last couple of months have been marked by the culmination of some discussions we have had with outside counsel and with the Treasury.

I am really happy to report to you and everyone that is listening that we have made it crystal clear now, and Treasury has confirmed, that we, PCORI, will be able to secure all of our funding, regardless of what might happen around September 30, 2019. We will be able to secure all the funding that is in the PCORI Trust Fund and dedicated to PCORI before that September 30 date if need be.

That means we can all be confident that if we fund a five-year study tomorrow, we will have the funding and be able to administer it through to the end. That is the message. We have had some concerns that some researchers may be wondering whether the awards we are offering could get curtailed in September 2019.

I am happy to say no matter what happens in

September of 2019, we have the funds. We are not over committing. We are not committing beyond the funds that we have available to us at that point. Important note.

The last thing is just to say on Thursday and Friday of last week, we had the merit review panels for the four targeted funding announcements, that on the novel coagulants, two on management of opioids, one on the treatment -- approaches to treatment resistant depression, and the fourth was on treatments for Multiple Sclerosis. Those review panels took place on Thursday and Friday.

My understanding is they went exceedingly well, and we hope that in July of 2016, we will have the largest batch of targeted funding announcement awards to present to the Board for approval, July, possibly some of them may drift into August. Really sends a clear signal of what PCORI is about and the kinds of comparative effectiveness research we bring to bear.

Today and tomorrow, the next round of pragmatic clinical studies are being reviewed and

the next round of broad clinical studies are being reviewed. This week in addition to being a Board weekend and week, it is one of the largest merit reviews we have had to date. The word is the proposal really are improving in quality over time. I just heard that last week.

Today, we will be talking about ways to enhance that, but it sounds like our efforts to date have already taken us in that direction.

Gray, I will stop and just see if there are any brief questions.

DR. NORQUIST: Before we go to the Dashboard, let's open it up and see if anybody has questions/comments. I don't see any.

Allen, are you on the phone?

DR. DOUMA: I am.

DR. NORQUIST: Go ahead, Joe.

DR. SELBY: Here is our --

DR. NORQUIST: Just let me say one thing. If you have the slide deck, you have more slides than Joe is going to show. I have been very clear, we do not want a lot of slides to talk to, so that

is why we asked everybody to read in advance. If you didn't, you will be behind, basically. We all agreed we would have much more of a discussion session than just being presented to.

DR. SELBY: We worked that with all our staff, and it is difficult. It is difficult to let go of those slides, but I think we have done a pretty good job.

DR. NORQUIST: Okay.

DR. SELBY: Here is our Dashboard. You have seen this, so I'm not going to say much. I will draw your attention to the two goldenrod or yellow sectors. Those are areas where we have fallen below our expected.

In the first one, it's the amount of money we have committed, not spent, but committed to research in fiscal year 2016, and you see by the end of the second quarter, the top line is the amount budgeted. That is maybe a bit extreme because it is adding up every award we announced and taking that top dollar. When we say "up to" $20 million, we put $20 million on.

You might logically think that we would fall somewhat short of that. The middle bar there is our historical record. That is where we have fallen to date, probably about 20 percent below what we announced.

What you will see is that in 2016, through two quarters, we are right at our historical performance, and we are again a bit below, not dramatically below, but a bit below, where we had budgeted.

That continues to be an issue and that is one of the reasons that we have all the application enhancement work underway that we do, and you will be hearing about that later.

On the upper right is the expenditures. Again, as has been the case in previous years, we are spending less both in research awards and in other categories, program and administrative activities, than we budgeted. Regina is going to go through that in greater depth.

One message is that whereas last year we were 28 percent underspent mid-year, this year we

are 18 percent. We think that is real, that is a real change, that as we reach steady state, as we reach a plateau, as we are not budgeting for people that take a little longer to recruit than possible, we are beginning to catch up.

The other things on here I will show in subsequent slides, a highlight on specialty physicians and PCOR, results on influencing the research of others and results on engagement and research.

This is just two examples, there actually are more, but this is a very nice one from the Journal Academic Radiology, the Association of University Radiologists, have a research alliance, and they reviewed all PCORI funded radiology projects, and there were a number of them, and described how the methodology standards apply in the area of medical imaging and diagnosis.

They also presented an agenda, which we are looking at carefully for future projects in the field of patient-centered outcomes research. You see the quote there, "As radiologists, we must

embrace PCOR or risk missing a key opportunity to demonstrate value and improved care."

In nephrology, Dr. Harold Feldman, who is at Penn, Director of the Center for Clinical Epidemiology and Biostatistics, is also the incoming editor of the American Journal of Kidney Diseases, and he said in his opening editorial -- he highlighted the major studies related to nephrology that PCORI has funded, and said the Journal is going to focus on translating findings from patient-centered outcomes research in the clinical practice.

Two nice examples of the way that others are talking about PCOR and PCORI.

This is a very nice example from the Meharry-Vanderbilt Alliance, Dr. Consuelo Wilkins, who is the Executive Director of this Alliance in Nashville.

PCORI is credited with being a catalyst for their decision to include community members and stakeholders in the scientific review process for their pilot awards, their CTSA pilot awards program. They observed PCORI's review process, decided it

could work for them, and they now have a training curriculum that builds from our own mentor program.

They also instituted a postdoctoral research fellow program in community engaged research, and they have a community scholars program for pre-doctoral students, where one can get up to $5,000 to support a research project on community engagement during your pre-doctoral period.

You will see Dr. Wilkins cited PCORI and PCORI funding as a catalyst for expanding their teaching in this area.

This is a nice publication in JAMA Surgery from a PCORI funded project where they talked about how the inclusion of patient stakeholders on their research team led them to change their recruitment rates and the script for enrollment, driving their enrollment rates in a PCORI funded trial from 65 to 95 percent. This is about a study of surgery versus antibiotic therapy in pediatric appendicitis, and this was about involving patients and their parents more actively in the decision.

This is a new page, and you are going to

see it. I think it is probably going to progress to the Dashboard pretty soon. These are our pragmatic studies, really our large flagship studies. There are now 20 of them, 14 of them, the contracts are underway, and 12 of those 14 were eligible for their first evaluation and you will see, using our green, yellow, red evaluation, 10 of the 12, the top bar, are on track in every way. Two of them are a little bit behind, and that is on recruitment.

The percent of the 12 projects that could be evaluated that are on track is 83 percent. The number of projects with recruitment milestones was just four, because it takes many of them a while to get up to date on recruitment, to start recruitment. Four of them -- two of them were on track with 100 percent of recruitment met, and two of them were behind.

The two that were behind are an interesting finding. One of them is actually taking some time to identify -- more time than they thought to identify the participating hospitals. The other one is having some trouble assuring coverage of in this

case genetic testing by the payers that are involved, and they are working hard payer by payer to get coverage for the genetic testing that would go into this large randomized trial of genetic testing surrounding mammography screening.

I think you are going to see more issues around coverage of particularly treatment that have not -- that are new and haven't been picked up by payers yet. That is going to be the subject of a Board level discussion soon.

In general, the projects are doing quite well, not surprising that two of them would have some problems of the type we just described.

This is PCORNet, and this is the number of research projects underway, most, although not all, five of them are funded by others, the rest are PCORI funded demonstration projects. You will see we are a little bit behind in quarter two, 10 funded versus 13 projected.

It is because of two things. One project has been delayed by the Selection Committee, who had some very legitimate concerns both about methods and

possible conflict of interest, and the other is the projects that got funded just turned out to be larger, so instead of funding 6, we funded 4. That is not really a shortfall in terms of spending, it is a shortfall in the number of projects, small, and the networks are engaged. You see 25 networks out of the 33 are already involved in at least one of the projects.

If you look on the left, the observational studies, those two darker blue studies are the two obesity observational studies, large studies. One involves 10 and one involves 12 networks. I think that is mostly CDRNs but there are some PPRNs as well.

The PPRN demonstration projects that are observational studies involve 7 PPRNs. The right cluster is randomized trials, adaptable, and involves, as you see, 7 CDRNs, and the other trials are PPRN trials. Most of the PPRN projects actually are randomized trials, and they involve from 2 to 6 PPRNs per trial.

From PCORNet, again, the front door policy

has been elaborated and approved by the PCORNet Council. The front door is the way that external researchers and external funders will approach PCORNet. This underwent want PCORNet likes to call a "soft launch" in April of 2016. That meant people who were already involved with PCORNet one way or another could approach PCORNet, and we would begin looking into the possibility of their study ideas.

You will see in the upper box on the right of the inquiries we have gotten, 13 have been about trials, 4 about observational studies, and 2 about to and from participating sites, inquiries from participating sites. The requesters include academics, industry sponsors, foundations, a national association, one Federal inquiry, and one that came from a research center.

The full opening of the front door will take place some time in the summer of 2016, probably at the very end of June/early July.

This is really extraordinary news. This is the state of readiness, the progress we have made in standardizing data across the DataMarts. The

DataMart can be one health system or a cluster of health systems that aggregate their data into an instance of the common data model.

In the box at the upper right, you will see in PCORNet at the moment, there are 83 DataMarts, 83 instances of the common data model representing one or more systems. This number keeps growing.

Just in the less than two months, from March 30 to May 19, you will see what we have is a progression from the very first interaction with the coordinating center, that is called the diagnostic query, to the data characterization phase where they run a substantial query sent out by the coordinating center to the first prepper research ready phase where the coordinating center actually says you are ready for pilot work to further dedication review.

That is back and forth with the coordinating center about findings in the data that have been sent, the aggregate data that have been sent to the designation as ready for research.

We have gone from zero ready for research to six. The number that are in that second, the

data characterization review, has grown. The numbers in that very first phase is shrinking, and I think really the reason you see them is because they found several other DataMarts, driving the total number of DataMarts.

This progress is just really knocking us over. We are very pleased. We have a target date at some point in the summer where all the DataMarts that are going to go forward need to be research ready. Right now, we are very optimistic that a large number will be, not maybe 83, but a very large number.

That is great news from PCORNet. Gray, that is it. If there are questions about the Dashboard, I am going to go back and put it up. Questions about what is on the Dashboard, but also as always, questions about what you would like to see on the Dashboard, how we could improve it further.

DR. NORQUIST: Francis Collins is up first.

DR. COLLINS: It was very helpful to have the review. This is Francis Collins, Board member.

I just want to go back to the main Dashboard, which you now have up on the screen. A question about how you set your benchmarks for research projects being on track or not. I think we have talked about this before.

When you see that less than 75 percent are actually, as far as enrollment, in the green zone, and only about 50 percent appear to be at 100 percent. I'm a little surprised that is then called "green," but it must reflect what you are setting as your benchmarks when you think you are hitting them.

This is obviously one of the big challenges of running clinical trials, and one that we need to watch really closely.

DR. SELBY: Francis, you made that comment last time.

DR. COLLINS: I am very consistent.

[Laughter.]

DR. SELBY: You are. We looked into it carefully, including calling NIH and other places. No one has this kind of data across their portfolio's. Nobody was able to tell us. As you

say, recruitment is a stumbling block for every funder and every trialist. We have said what we are going to do is monitor the trend, and we take heart in the fact that the trend is holding steady or going up just a bit over time.

To say that half of them are at 100 percent recruitment is probably in our view and based on conversations we had with others, as good or better than others are doing. I don't think we are going to find anybody else who is tracking it the way we are to say at our place, 62 percent of the trials are on target. We have not been able to squeeze that out of any other funder yet.

If people have suggestions for someone to talk to to get a benchmark, we would be very appreciative.

DR. COLLINS: I just think it would be good if you established what your own criteria are for green, yellow, orange here, because it has not been clear to me exactly what you are going to consider to be in each of those categories, and going forward, it would be helpful to have that, even if

you can't find industry or community benchmarks, what is our benchmark.

DR. SELBY: It is in the ancillary slides. We have shown it a few times.

UNIDENTIFIED: Slide 23.

DR. SELBY: It's the table of green, yellow, orange, and --

DR. NORQUIST: Red.

DR. SELBY: Red, thank you, in the ancillary slides. We have shown it before. There are exact numbers put on the recruitment rates, like above 75 percent and 50 to 75 percent.

DR. NORQUIST: Number 23 has the columns so you can see. Leah?

MS. HOLE-MARSHALL: Following on that, on my Board deck, 24, is this the trend, how many are in yellow, orange, and red? I think as I understand this slide, you're monitoring the same number from quarter to quarter, and just adding the projects that were added, that were approved, right?

DR. SELBY: Yes.

MS. HOLE-MARSHALL: It is a cumulative

number from quarter to quarter.

DR. SELBY: Yes.

MS. HOLE-MARSHALL: It looks like approximately, the yellow, orange and red stay about the same. In our definition, if they are red, they have 30 days to remediate.

DR. SELBY: They can come back into green, so ones that were yellow, orange, or red can work their way back up the spectrum.

MS. HOLE-MARSHALL: Are the red's from quarter to quarter all different projects?

DR. SELBY: I don't have that at hand, Leah. Projects do get terminated, so I would say undoubtedly the four in quarter two of 2016 aren't the same as the four in quarter three of 2015. There have been some projects that have been closed in the red category.

MS. HOLE-MARSHALL: I guess I have different numbers. If the red is 30 days, that is our definition, they have 30 days to get out of red. I just wonder how many of those are cycling out. It looks like they are consistent over time.

DR. SELBY: I can get you that number again.

MS. HOLE-MARSHALL: Those are cumulatively. Cumulatively, we have terminated four, not quarter by quarter.

DR. NORQUIST: On mine, I think that four applies to the orange line. It looks like the black line, which is terminated, is zero. I don't see any terminated, do you? Is there one?

MS. HOLE-MARSHALL: On the bar side, 24 is one.

DR. SELBY: It must be one.

MS. HOLE-MARSHALL: Just in terms of the trends that we are watching, maybe some detail around the ones that are red, orange, and yellow and how they are moving. I don't know exactly how to talk about that, but I would expect some would move up, meaning move from either red or orange to yellow or green, which is great. Some would move down and some are staying the same.

DR. SELBY: Very good, I think that is an excellent suggestion. We will definitely bring it

back with the next quarterly report if not before.

DR. NORQUIST: Other questions on the Dashboard?

MS. HOLE-MARSHALL: I had one more suggestion on the Dashboard for PCORNet, and that is thank you for the information about the DataMarts and readiness. I think it is really helpful and exciting to hear that progress.

We had talked last time about the queries that we had asked to be able to run, and as part of our proof of concept, it's important to show that we are making progress actually on results of those queries, so it will be useful to have a similar graphic next time on the number of queries that were expected and how we are doing on that.

DR. SELBY: Good.

DR. NORQUIST: Bob Zwolak?

DR. ZWOLAK: Bob Zwolak, Board member. Joe, I really appreciate the Dashboard. I think it gets better and communicates better each time that we see it. My question relates to the top left yellow bar. In one of my day jobs, I spend a lot of

time trying to smooth out peaks and valleys of demands to optimize resource utilization.

It strikes me that here for quarter one, we have no commitments and two and three are small, then quarter four in particular this year, in July, there is going to be simply an enormous announcement.

The operational question is in this world of grant making, is this created by design that all the announcements would be sort of into the fourth quarter or would we do better if somehow we were to smooth out the grant announcements?

DR. SELBY: That's a question that is under active consideration. The reason quarter four is so large is almost completely because of the four targeted funding announcements, each with many millions of dollars at stake, that were released on the same day last fall, and they all come due. That balloons quarter four.

We are talking about ways to even out the funding. I just told you about the incredible amount of merit review work this weekend, and the

question is on the table.

I think there are pro's and con's to bunching things like solicitations and merit reviews. There definitely are con's, and folks in the science group are talking increasingly about the con's of doing it that way. So, more to come on that.

DR. NORQUIST: I think the other issue, Joe, is going to be the staff time. We don't want to have a delay in getting the awards out because the staff is overwhelmed getting the contracts and things out at a particular time. That's just something else to think about.

Andy?

DR. BINDMAN: Hi, Andy Bindman, Board member, and in some sense a newbie here. I'm going to ask questions that perhaps have already come up. First, I want to say how great it is to have a Dashboard like this. I really commend the work for all of you for putting this together.

DR. SELBY: The Board made me do it.

[Laughter.]

DR. BINDMAN: I just want to think about some of the themes that I think are so important for PCORI, and I'm trying to figure out where it would be extracted from the Dashboard, things like -- it seems like it would be possible from this, but I'm curious how you would think about the Dashboard supporting ways of knowing the speed at which conducting research is enhanced relative to some other traditional approach.

Second, the speed at which the evidence is taken up and used to change practice, how that might be reflected in some of these measurements, and also the degree to which or how the research is impacting the communities' ability to further explore the clinical area that it is working in. What is it doing to enhance the capacity.

I know there is a box down there called "Impacts," which you are coming to. I assume that is mostly at the front end of the patient and changing practice. I'm trying to think about the sort of speed issues and the process and how that may or may not be reflected in the Dashboard, and if

there are ways you think it can either be extracted from what you have here or perhaps additional ways of measuring that that could give you insights, because those are important outcomes, I believe, of PCORI's agenda.

DR. SELBY: Good, thanks. We will look into that notion of speed. One thing is you can see in the left box in the middle row, the final reports received when expected. You will see that we are really doing pretty good at getting the final reports in when expected. I will say a lot of those, not all of them, but a number of them did negotiate a year extension. With that year extension, they are coming in. That's not exactly speed, warped speed.

You will also see from this that high jump, Andy, in quarter four of 2015 are the pilot projects. Our initial projects that we let in 2011, in fact. We are just beginning to see our CER work coming up. I think in the fourth quarter of 2016 and the first quarter of 2017 we will see a very large jump. At that point, we will be able to start

talking about dissemination efforts, implementation efforts in those studies.

DR. NORQUIST: I think the other thing is on this particular Dashboard, one of the things, Andy, we used to have a very complicated Dashboard, with 5,000 things on here, so we got them to narrow it down. There are other things that are not on here, like engagement awards, some of the uptake they are measuring and things like that about things that have already been published.

There is some of that in the background, and even those particular metrics are not up here right now, although they are in that total slide deck. It is a good point about the speed.

Steve and then Francis, and then we will have to close this session.

MR. LIPSTEIN: Andy, just through the lens of somebody who is leading a health care delivery system right now, there are so many things that are influencing and changing practice and the pace that it would be hard to identify our patient-centered outcomes research influenced at -- it is not a

controlled experiment.

Even if we could measure somehow dissemination uptake, it would still be hard to attribute it specifically to PCORI funded initiatives. There is just a lot going on out there right now. I don't know how we would run the controlled experiment.

DR. NORQUIST: Francis, and then Barbara will have the last word, and we have to stop.

DR. COLLINS: Just picking up on a comment that is on slide 33 about benchmarking indicating that late or non-submission to clinicaltrials.gov is high, that is a problem, and that clinicaltrials.gov, a final rule is going to be issued probably fairly soon, and this will then make a very stringent requirement for that to be met.

Obviously, PCORI grantees ought to be leading the charge to be compliant with that, given how hard we have worked to try to be sure that information gets deposited.

DR. NORQUIST: Thanks, that's critical. Barbara?

DR. McNEIL: Great Dashboard. This comment isn't necessarily designed to change the Dashboard, but it does pick up on a comment that was made, how do we know we are making a difference. I wonder if internally we want to do the following, two things actually.

One would be to get a sense of what the impact factor is -- actually not a sense, actually get the data on what the impact factor is of the various journals that our articles are being published in. If they are being published in high end journals, that's a big deal. The second one is what is the citation count for each of the articles published.

I think both of those would help us a lot in determining whether or not we are making a difference. If something has been cited a lot, it probably means it is getting out there and that would be a big boom to understanding how good our dissemination really is.

DR. NORQUIST: Okay. Regina? I'm sorry, Harlan?

DR. KRUMHOLZ: I just want to make two quick comments. One is building on what Francis said. Even if the rule is coming out, I think it would be great if PCORI were to dedicate itself to being prepared for a press release on the data that comes out.

That will take a little pre-work in order to do that immediately. We are going to be 100 percent in compliance with the Federal rule, we are going to be completely aligned with the NIH, and we applaud the movement towards registration.

Rather than react and take a month to do that, we could be prepared now so that within 24 hours we are coming out with a press release. I just wanted to request that we put in place whatever needs to be done. RTC can talk about that tomorrow, I think, in the open science part of the agenda, but it would be great to be posed to do that.

I think with regard to what Barbara brought up, it just opens up this larger thing, which I think at some point we could do, which is how do you judge impact of science. I personally am one who

believes the citations are just one narrow way to do that, but there are many other ways to do it.

It might be nice for PCORI to lead the charge on trying to think about that, with a position piece. It is something which we can incorporate a lot of different directions about the way in which science can help make a difference, and a way PCORI could provide some fresh air into this current debate or understanding would be wonderful.

DR. NORQUIST: Yes, I think more than just the citations. The citations are scientists referencing each other, whether that actually plays out in the real world is a whole other issue.

All right. In the next session, we have the mid-year financial review. Larry, Regina, I don't know which of you wants to go first. Thank you, Larry, the Chair of our Finance and Administration Committee, Larry Becker and Regina Yan, who is our Chief Operating Officer, are doing this session.

MS. YAN: We are here to brief you on the mid-year financial review. We will be going over

our revenue and cash balance as well as all the funding commitments that we have made. We will also review with you our budget versus actual for the first six months of the year.

I want to say in previous years we reviewed with you the five months actual, and this year, we are able to actually improve our system and are able to cover six months with you.

We will also look at the top drivers, key drivers, for the variance, and we will be looking at our funding commitment plans for 2019 as well as our estimated revenue and expenditures.

In the beginning of the fiscal year, we have $816 million of cash balance, most of that is in the Trust Fund with the U.S. Treasury, a small amount of it is in our operating bank account.

During the first six months, we have revenue of $214 million, $120 million is in Federal appropriation, $98 million in CMS transfers. We have a negative adjustment of PCOR fee, mainly because the adjustment between reconciling the actual versus the estimate that is usually

transferred to us in August, that conciliation is done in March, so that is reflected in our six month financials.

We also have interest income of $700,000. At the end of the second quarter, end of March, we have a cash balance of $871 million.

All these funds are pretty much obligated because we have made funding commitments of $1.3 billion, which would be paid out through -- right now, we have one award that is through 2021, so these payments will be made throughout the life of those projects, and we have made payments of about $400 million, but we have $936 million to pay out for all the projects we have funded so far.

Let's take a look at our 2016 budget and also our six month budget versus actual. We know the variance has been an issue for us the last couple of years, mainly because we have so many new activities and we didn't have a lot of historical data that we could go by.

Last year at this time I was presenting to you in the mid-year financial review a variance of

budget versus actual at 28 percent, and this year, we are right now at 18 percent. That is still not meeting our target because we have set a target for ourselves of 15 percent, but I think we are going in the right direction, so we are very pleased with the progress we have made so far.

For the first six months, the budget is $174 million, actually, it is $143 million. You can see as far as award expenses is concerned, the variance is 14 percent. Our biggest variance is in program support. I will talk about the details in a few minutes.

Program support covers like expenses related to the Methodology Committee, our science department, evaluation analysis, research infrastructure, which is PCORNet, engagement, dissemination, and contract management.

Some of that has to do with some lack in personnel costs. We also have some activity that gets delayed. We also have expenses that we budgeted and we found we no longer need that, for example, some funds for a database that we no longer

need because we can incorporate it into our bigger database.

We have 21 percent variance in administrative support. Part of that is because we have budgeted some contingency for additional office space where we have not needed to acquire additional office space. At this moment, our variance is 18 percent.

If we look at the 2016 budget, our budget is $423 million, that's the budget that the Board approved, and the breakdown is among three major categories, one is award expense, 8 percent, program support, 13 percent, and 9 percent, administrative support.

If we look at the mid-year point, six months into the year, the proportion between these three categories has not really changed that much, so our expenditure in awards is 78 percent still, and program support, 11 percent, and administrative support, 11 percent. This is one thing we do monitor because we want to make sure that we keep that percentage, which is what we are targeting for.

A couple key drivers in the variance. Even though award expense, 14 percent variance, it is 78 percent of our total budget and total expense, so as far as dollar amount is concerned, the majority of the variance comes from award expense.

We do have some personnel costs, mainly of some of the vacancies we are in the process of filling, and we have some program activities that are being pushed back. The rest is miscellaneous expenses. As I mentioned earlier, there are some contingencies that we have budgeted that we don't need to use.

We continue to realize a lot of economy in our meeting expenses as well, and also even though sometimes we meet expenses for outside external meetings, when it is inside, we can actually host a meeting in-house, in our facilities. We do that so we realize economy there as well.

This is something you have looked at quite a few times. This is just to remind you of our funding commitment plans for 2019. Our plan is to commit $2.5 billion, 84 percent of that will be in

research, 11 percent, infrastructure, 5 percent in engagement.

I want to point out that within that research, that research also includes PCORNet research, so all the PCORNet demonstration is considered research, that goes into the research column, and what you are seeing, the 11 percent is basically just infrastructure support.

DR. NORQUIST: Evelyn has a question.

MS. YAN: I'm almost done.

DR. WHITLOCK: Just a question, under which category does the dissemination and implementation appear?

MS. YAN: Right now, we have not included that in this table, but we will be doing it in 2017 because starting next fiscal year, we will have major dissemination activities.

DR. WHITLOCK: When you do, under which of those categories?

MS. YAN: It will be a new column. We will be adding a new column.

DR. WHITLOCK: So, it's not accounted for

in the $2.5 billion?

MS. YAN: No, it's not. In the next slide, you will see that showing up. Here it is.

Our total projected revenue is $3.2 billion, and we talked earlier awards are $2.5 billion. We have a little over $100 million in dissemination, which is 3 percent of our total revenue and expenditures, it is about 4 percent of total awards, and $310 million in program support, and $278 million in general administration.

If we break it down, it is about 79 percent, close to 80 percent, in award spending, 3 percent in dissemination, 10 percent in program support, and 9 percent in general administration. This is what we are projecting through -- with the revenue that we know for 2019.

Of course, our expenditures would be spent out through 2024 because that is the time line we are looking at if we are going to make awards in 2019, in order for us to support those projects through the end of the life of those projects, looking at 2024. That is the operating time line

that we are looking at.

Any questions?

DR. NORQUIST: Wait a minute. Larry?

MR. BECKER: Just a couple of comments. First of all, thank you very much because over time, as you all know, we have gotten finer and finer in terms of being able to predict these dollars, being able to account for these dollars, and that is Regina's team doing that, and on your behalf, Christine, Bob, Kerry and I review this with the team monthly.

We get to review these dollars on your behalf and make sure we have those accounting pieces pulled together. Kerry on governance has the Audit Committee. You know the prior audits have all been very, very clean. We are watching that on your behalf. We have very sound financials.

As Joe mentioned, the great work that the team did to assure that we are able to get the dollars to PCORI that have been committed through this whole process by the end of our current legislation so that we will be able to deliver the

dollars to the researchers that we have committed.

Finally, understanding all of this, clearly, we need everybody's help, all the committees, to make sure that we are moving the research, we are being able to do the kinds of things that we are budgeting.

You can see, if you have followed the last couple years, we are getting closer and closer. Regina reported about an 18 percent number. We are making great strives in being able to predict what we are going to extend, how much, and to be able to budget that.

Thank you to the team and thank you to the entire staff to be able to get this engine moving, because it's been a long road these last six years to do that. I think we are there and I think we are starting to really hit on most of the cylinders.

Questions?

DR. DOUMA: I have a question.

MS. HUNT: Gail Hunt, Board member.

DR. NORQUIST: One second, Allen, Gail is next.

MS. HUNT: I'm a little dismayed at the 3 or 4 percent of the budget that's going for dissemination, and that is going to be in 2017, as you mentioned. I've been concerned all along that we include implementation along with dissemination.

It seems to me we are getting short shrifted, and we need to perhaps think about how we could expand that and think about ways other than, for example, citations and journals, that we can move dissemination to actually getting the result into the patients' hands and the primary care doctors. I would just appreciate some discussion of that.

MS. YAN: I think this afternoon, there is going to be a presentation.

DR. NORQUIST: Yes, we are going to have a discussion this afternoon.

MS. HUNT: The discussion that we're going to have, does it make it available to us to say we should have additional funding that is moved into that category?

DR. NORQUIST: I think we can have that in

the discussion, we can have a conversation about where we move from that point. Allen, it's your turn.

DR. DOUMA: Thank you. I'm trying to interpret --

DR. NORQUIST: Allen Douma, who is on the phone with us.

DR. DOUMA: Allen, Board member. I'm looking at the numbers with regard to the number of unfilled positions, and it looks like there could be as many as 45. Is that correct? Or will be as of April 2016 when 31 new positions open up.

Do we have 45 unfilled positions, and if we do, what does that mean with regard to our productivity and with regard to budgeting for new positions in 2017?

MS. YAN: Allen, at the end of the second quarter, we did have 40 some positions. Most of them are the new positions approved for this fiscal year to be filled in over time. We also have some turnover, which is a normal thing in organizations, so we are also filling those positions.

Right now, we are filling about 5 or 6 positions on a monthly basis. I think we continue to make some good progress. Sometimes, some positions take a little bit longer than others.

DR. DOUMA: What is our turnover and is that comparable to what we would expect, or is there some greater challenges because of our funding issues?

MS. YAN: In our operations benchmark, on Dashboard, the turnover benchmark is 15 percent, which is looking at the industry average. We are right now at about 14 percent.

DR. DOUMA: Okay.

DR. NORQUIST: Any other questions?

[No response.]

DR. NORQUIST: Thanks, Regina, very much, and Larry, and the FAC, for the work you are doing also on this. As always, if people have questions or comments in the interim, please get back to Larry and Regina about that.

We are just a little behind. Robin, you have the Methodology Committee update. Robin

Newhouse is the Chair of our Methodology Committee and will give us an update on the Methodology Committee.

DR. NEWHOUSE: Hi, good morning. This is Robin Newhouse. I'm going to update on the Methodology Committee activities.

I'm just going to begin. Andy, I will give you all the credit for thanking you for giving us such a wonderful designee from the Agency for Healthcare Research and Quality, and we are happy to welcome Stephanie Chang, who is Director of the Agency Healthcare Research and Quality's Evidence-Based Practice Center Program.

She actually received her Bachelor's and her M.D. from University of Michigan, and received postdoctoral training and MPH from Johns Hopkins. She is trained in internal medicine and pediatrics at the University of Minnesota, and is a Board certified physician in internal medicine. We are looking forward to having her join us as we begin the following activities.

In terms of an update, I'll update you on

the implementation of the methodology standards as well as the public comment period for the draft revisions to the PCORI methodology standards, talk a little bit about how we are coordinating with the Clinical Trial Advisory Panel, and then finish with a couple additional updates, including network research methods work group update, as well as consideration for MC advisors.

To get started, implementation of the methodology standards, when we think in terms of implementation of these methodology standards, number one, we are interested in helping investigators understand and use the standards.

Second, we want to establish a system to ensure the integrity of research projects so they are of high quality, and also understand the barriers to use of the methodology standards.

In terms of helping others and researchers understand the use of the methodology standards, there have been a number of activities that have already occurred. In 2013, after the methodology standards were adopted, there were a number of

webinars, to be followed by face to face outreach conferences every three to four months across the nation in 2014. In 2015, the online continuing education program was launched, and in 2016, an academic curriculum was added.

In terms of using the standards to ensure the integrity of funded proposals, the methodology standards are integrated throughout the process, from the letter of intent template to the full application. There has also been extensive training not only of the PCORI staff but the merit reviewers.

There is a review of the study protocol for adherence to the methodology standards, as well as the PCORI staff are working carefully with the funded investigators and teams in their progress reports to assure compliance with the PCORI methodology standards, and the standards are also included in review of the final research report.

I just want to pause to say I give the PCORI staff a lot of credit for this intense activity who have continued to monitor from the beginning of the adoption of the methodology

standards the use in PCORI protocols, and when Joe talked in the Dashboard about the quality of the PCORI studies, I have to say this is part of this whole process.

In terms of uptake of the methodology standards, these are three graphs. The first one on the left is CME/CE certificates. Of course, that was launched in the fall. These are six modules that are available online. The use has been pretty high, so the first bar was in the first quarter it was launched, 72 certificates were issued. With this second bar being until March, so 32 certificates were issued.

The major users of the certificate are physicians and nurses with some being awarded to pharmacists, physician assistants, and other participants.

In terms of citations, the next bar graph is related to our publication in JAMA in 2012 when the methodology standards were released, and that publication has continued to be highly cited.

The last bar graph is related to the web

views of the methodology standards, and you can see there was a peak in the fourth quarter of 2015, but the methodology standards continued to be highly accessed via the Web.

The next agenda item is public comments. We have revised all of our current methodology standards, those methodology standards were posted for public comment between January and April of 2016.

We received a total of 84 comments to these methodology standards, and we also had one new standard, and that is designs with cluster, 84 comments were received, mostly from health researchers, industry, also caregivers, family members, and patients.

These public comments will be guiding the final revisions of the methodology standards that we bring back to the Board for approval.

In terms of what the public comments were related to, you can see that most of the comments were related to formulating research questions, patient-centeredness, data integrity, and rigorous

analysis, and causal inference. Each one of those comments, as I mentioned, are being reviewed for incorporation into the revisions to the standards, and will be discussed and reviewed by the Methodology Committee before coming back to the Board.

Another area of activity relates to our relationship with the Clinical Trials Advisory Panel. You may remember that the Clinical Trials Advisory Panel advises PCORI, PCORI staff, and the Methodology Committee. The work of the Clinical Trials Advisory Panel comes through the Methodology Committee.

There is close collaboration. We have members from the Methodology Committee that serve and act in an ad hoc role on the CTAP. They have been involved in a number of activities including advising on strategies for PCORI clinical trials, and they are responsible for also advising on guidance for the conduct of clinical trials, as well as developing position papers.

There are complimentary activities of the

Methodology Committee and CTAP. The Methodology Committee, of course, is responsible for updating the methodology standards, creating methodology standards, and dissemination of methodology standards, where the Advisory Panel on Clinical Trials has been working on activities such as selection, research design, implementation, and technical issues related to clinical trials.

They have a subgroup on recruitment accrual and retention subcommittee, as well as standardization of complex concepts in their terminology subcommittee.

Some of their work and recommendations related to recruitment, accrual and retention will be coming to the face to face meeting this week.

You may remember that on December 10 there was a workshop, Data Quality and Missing Data Expert meeting, that report from that meeting has been posted.

There are a number of activities that are planned in follow up, including potential guidance and standards, webinars and workshop, and

collaboration with PCORNet. There are a number of Methodology Committee members that are involved in carrying this work forward.

The last item that we have been considering is related to appointing advisors to the Methodology Committee. You may remember that Dr. Clyde Yancy and Sebastian Schneeweiss rotated off the Methodology Committee. We have considered what other expertise we need on the committee, and are also considering appointing a couple of advisors to join us.

With that, I'll close, and invite any questions that you may have.

DR. NORQUIST: Thanks, Robin. Gail, is that your card up? Others? I know Allen Douma is on the phone, and I think Harlan Weisman is also joining us by phone now.

DR. WEISMAN: Yes.

DR. DOUMA: Yes. I'd like to ask a question.

DR. NORQUIST: Okay, go ahead, Allen.

DR. DOUMA: Robin, on your chart, when you

show the web views by quarter, do you have a breakdown of what a web view actually means? Is it simply somebody clicking on the front page of something dealing with methodology, or does it have to do with people downloading anything? Do we know what that web view means?

DR. NEWHOUSE: I'm going to have to defer that question.

DR. DOUMA: Okay. Just a follow up to that, I think the methodology standards is a huge and important sentinel project for PCORI. I'm concerned that it looks like we are sort of petering off with regard to making people aware of it and its value. The CME/CE certificates, given the size of the universe, seems relatively small.

Can we talk about how we can promote this better/more in the future than we have been?

DR. NEWHOUSE: I do think you're right, it certainly has been disseminated broadly to a number of the dissemination networks, but the uptake, I'd have to say, 100 certificates actually sounds pretty good for a start, but there are marvelous, I think,

learning opportunities. They are incredibly well done. We do have to figure out how to make sure that people are aware of what an opportunity this is to learn about the methods.

DR. NORQUIST: One question on that, Robin, as a follow up, CME certificates, that's one thing, but we talked before about the classes or things, academic institutions, schools of public health where people are teaching this. What sense do we have about that, whether any of that has been incorporated in curricula around academic sites or things like that?

That actually is more important in some ways than how many people log in to get a CME certificate.

DR. NEWHOUSE: Yes. I would say the path is sort of dissemination through the networks as one thing, but getting out there to help people realize how it can be used will be the next step, being a little more active with the dissemination.

These are incredible resources, both the academic curriculum is new, just launched this year.

It is well done. There are training materials. There are PowerPoint slides. There are questions that academics can use when teaching around method standards. We need to do some more work to get the word out.

DR. NORQUIST: I think that's a golden opportunity, and particularly perhaps at meetings where methodologists are, things like that, there could be an option to do a presentation or something.

Leah and then Barbara.

MS. HOLE-MARSHALL: Thank you for that. This is amazing, and I do think it is a sentinel project. We are first on the lead with the product and now we are actually seeing it put into place and used. I think that is great. There is the hope that we can continue to expand how many people are exposed to it.

I wonder if there is any way we could get either through a survey or interviews data about whether individuals -- we did acknowledge these were some baseline or minimum standards, and I wonder if

folks are feeling like I know this part, and how much of it is that, whether or not they actually apply it and do know it, that they are feeling like I know I have to comply with that, but I think these are basic and I already agree with them, so I don't need to be instructed in them, versus I'm just not interested in this area of research or I didn't know about it.

It might be interesting for us to see where the potential uptick really might kind of change the mindset about that, depending on what the issues are. If there are staff available to do key interviews or surveys, that might be helpful.

My second question was on NO1 trials, and I don't know if this has been discussed with the methodology group, but it has come up in other areas of PCORI, and it would be great to get some guidance on that, just putting that out there for the Methodology Committee to talk about.

DR. NEWHOUSE: Thank you, Leah. I would say that the PCORI staff has done a lot of work in terms of surveys. We can certainly include some

more questions, and also understand how the merit reviewers are finding use of the methodology standards as well. Yes, the NO1 trials has been a topic of conversation, so more to come.

DR. NORQUIST: Barbara?

DR. McNEIL: I think this is great. I just have one question in terms of making our product known better. Robin, do we have any sense what parts of our methods -- I haven't looked at them very recently -- are not covered in the routine biostatistics books or course material that our Master level or graduate students would have access to? What is there that we have that is quite different that we could say ah, if you try to look at textbooks 1, 2, 3, 4, 5, they all have it but not quite in the same way as we do.

Just wondering when investigators come to look up -- I'm not sure what kind of analysis they would be doing, they would first pull out whatever the statistics book of the year is. I know what it was in my generation, but I don't know what it is now. That may be a reason for somewhat of a fall

off or perhaps not an uptick in the use of these.

DR. NEWHOUSE: The methodology standards were not intended to be standards where there was a lot written and it was well adapted or where there was nothing written. They were targeted where there was theoretical or evidentiary basis for the standards. That's the only answer I can give in terms of the basis for the standards in the textbooks at the time, so there was something there related to the standard or it was theoretical.

Mike is raising his hand.

DR. LAUER: I think it is much more than statistics. Having been involved with putting these together, it covers the entire gamut of research, how it gets put together, how it gets designed, who gets brought into the process, what are the things you have to think about, and analysis is just one part of it.

I think that is what is particularly appealing about the standards, that they are so broad-based and comprehensive.

DR. NORQUIST: Barbara, anything else?

DR. McNEIL: I think that's fine, but it's a little bit of a subtle distinction for the person on the street, to be honest, who is putting a grant together.

I'm just wondering if there is a way to -- if I were putting in a grant to PCORI on comparative effectiveness on diagnostic test A versus diagnostic test B, I'm not sure that our method standards would be the first place I would go. It may be the first place I should go, but I don't think it would be the first place I would go.

I'm wondering if we could make that distinction a little crisper. Maybe I'm imagining things, and this isn't a real point.

DR. NORQUIST: Is this a separate point? Okay. Harlan?

DR. KRUMHOLZ: Just quickly, Barbara, you are raising a really good point that we have discussed before. One of the questions was whether or not in a standard request there ought to be guidelines, to go along with the application that say did you do this, this, and this, or if you

didn't, how did you depart from it.

We have so far resisted that, incorporating that in the applications, but I think it is worthy of discussion. I don't know where it goes. It should probably go to a subcommittee first to consider.

Barbara, you are raising a really good point, and I think the great content to the methodology report isn't necessarily positioned to optimally influence the applications, and it would be up to us, I think, just to bridge the tools from the really great content and create the enabling structures that say you want to put in this grant the grant is sufficiently structured so it means we are looking for work, and then this is the document that is the information, and this is the form that should be at least checked.

I want to balance that with we don't right now have the greatest reputation on the street with our user experience with regard to our applications, so it is about the balance, I think.

It's hard, not overly burdening the

application but to do it as an enabling structure, it is a question of how it gets done. We probably would want to talk with applicants, too, as a constituency before we implement something like that.

DR. NORQUIST: Freda?

DR. LEWIS-HALL: Actually, I have a follow on to Harlan's comment, which is I wondered whether or not if we were able to do that, we could actually pull it through to other review committees. That would be a dissemination platform unto itself.

If non-PCORI funders were in addition to PCORI funders, and we could find a way to give this consideration without being over burdensome in a process, then we would not only affect those that were seeking PCORI funding but we would be able to perhaps transform what happens in other places where funding is provided.

DR. KRUMHOLZ: A quick add on to that. When NIH said here are the five areas that the study section is going to pay attention to, you know when you submit a grant to NIH, you hit each one of those

five areas or you risk not getting funded.

That clarity and ours could have a little greater specificity. It is like we said in the beginning, move the food and people will follow. It will make a big difference.

DR. NORQUIST: Rick, and then we will come back to you, Bob, since yours is different.

DR. KRONICK: I just wanted to add that we had the same questions, Barbara, when we were actually making the initial methodology report, which is what novel contributions is this going to have to existing standards and traditional approaches.

The answer is we weren't going to contribute anything novel, what we were going to do was emphasize key elements of rigor that would be required by PCORI, and also emphasize the notion that we wouldn't be getting funding to traditional researchers who would have had Master's in biostatistics and epidemiology, but this would be a single go to approach to say this is why we emphasize missing data, this is why we emphasize

patient reported outcomes rigor, these are the five different models of comparative effectiveness research, so there is one kind of source one can go to.

It wasn't exposed necessarily to traditional methodology, to understand what we emphasized, and then could potentially reach out to experts who were more familiar with those areas.

DR. NORQUIST: Thanks. Bob, another topic?

DR. ZWOLAK: Thanks, Bob Zwolak, Board member. That was a very nice presentation. Over the past month, Evelyn Whitlock has been enthusiastically trying to educate me about a method called "individual patient data meta-analysis," and I must say her efforts have only been modestly successful.

The question is I don't see too much in our standards for that, so it leads me to ask about whether there is an existing portal through which investigators or members of the committee can offer new methods that might be analyzed and added.

I know we are looking at some now, but is

there an ongoing approach for new suggestions?

DR. NEWHOUSE: Yes, there is a portal where we review those recommendations about quarterly, at least when we are ready to develop a new set of standards. We also get input from the field, conferences, those kinds of things, but there is a portal, so anyone can nominate a topic.

I would also add we are delighted to have Evelyn, she is very interested in those methods as well. Once again, another topic for the Methodology Committee and more to come.

DR. NORQUIST: There are no more comments. Thank you, Robin, and the Methodology Committee. A lot has been done from the days when we first organized, all the work you guys have done. Thank you very much, and we look forward to more.

The next topic that we have is consideration for approval of PCORNet Cross-PPRN Research Project Award. Before we get started on this, Joe and Rachael are going to do this, I just want to note that several people are recused because of conflicts of interest from discussion about this

and voting, and those people on the Board are Debra Barksdale, Steve Lipstein, Alicia Fernandez, Barbara McNeil, and Andrew Bindman.

I'm just saying it first in case you start asking questions in the middle of the presentation, and you are not supposed to do that. Rachael, are you going to do this?

DR. SELBY: I will just thank Rachael for presenting, and just remind you this is the last of the PPRN demonstration projects, they came in with a number of individual ones, which have been reviewed and awarded, and this is one that all 20 PPRNs came in on together. I thank Rachael for making the presentation.

DR. FLEURENCE: Thank you, Joe and Gray. The consideration for approval here is as Joe said, the last PCORNet/PPRN demonstration project. It is the cross demonstration project which involves all the current PCORNet PPRNs.

The purpose of this PSA was to allow the PPRNs to have an unique opportunity to broaden the scope of their research to include topics that were

meaningful to the larger participant community across PCORNet. PCORI sought to fund a comparative effectiveness research project that would demonstrate scientific, administrative, and operational capacity for collaboration across the PPRNs.

This project also had to address a comparative clinical research question that reflected the shared information needs on decisional uncertainties commonly faced by the collaborating PPRN community. In other words, looking for a question that would be of interest to a broad range of populations across the country.

This is the project we are proposing. The project title is "Healthy Mind, Healthy You." The research question is what is the comparative effectiveness of two online evidence-based approaches to using mindfulness to improve wellbeing.

The comparators, one is the eight session mindfulness- based cognitive behavioral therapy, also known as MBCT, compared to a three session

mindfulness light approach to mindfulness. The study design is a prospective randomized comparative effectiveness trial, and the targeted sample size is 8,500 patients.

The length of follow-up time is three months. The total budget is $4 million. All 20 PPRNs are collaborators on the project. It will be led by MoodNetwork PPRN, which has deep experience and expertise in running multi-site clinical studies in the area of mental health.

A few more words on the study. The outcomes that will be collected are well-being, which is the primary outcome, but they are also collecting perceived stress, anxiety, depression, psychosocial functioning, quality of life, and mindfulness.

The specific aims are to determine whether the brief three session mindfulness light intervention compared to the standard eight session MBCT intervention will improve well-being in the PPRN participants.

A second aim is to explore the

heterogeneity of treatment effects with both interventions, and a third aim is to contribute to the PCORNet Commons, a number of tools and resources that will be developed through these collaborations, and that was an important goal of the PSA as well.

The potential impact is to help determine whether a standard intervention such as the MBCT, the eight session one, compared to the brief mindfulness approach can have a clinically meaningful effect on individual participants' stress and well-being.

Some examples of contributions to the PCORNet Commons involve Web-based intervention tools for managing stress, depression, and anxiety, as well as lessons learned regarding governance, data, engagement, and dissemination for cross-PPRN research.

The slate overview is presented here. It is $4 million allotted and the proposed total budget is $4 million.

DR. SELBY: I don't think you said this, Rachael, but like all demonstration projects, this

is a combination of science and some work such as contributing this work to the Commons, which really falls more under infrastructure, but just enhancing research readiness going forward, and this topic has been reviewed and approved by the Selection Committee coming to the Board meeting today.

DR. FLEURENCE: That's correct. I think one of the key demonstration aspects of this project is the PPRNs are communities of engaged participants, patients, caregivers, families, and whether they have already signed off to participate in research, and the question is whether this PPRN community can through outreach and engagement actually recruit 8,500 patients in fairly short order. That is going to be an important proof of concept on the PPRN front.

DR. SELBY: Before we move to a motion and vote, any discussion? Larry?

MR. BECKER: Aside from the literal project, what does this hope to demonstrate about PCORNet?

DR. FLEURENCE: I think on the PPRN side,

it has been sort of very clear how we were moving forward in terms of developing the data infrastructure and also the operational and administrative building blocks to conduct research in a way that was different.

On the PPRN side, I think we have been searching for what these proof of concepts would look like, and I think the first demonstration is to show sort of how collaborative communities can come together as they did, all 20 came together to collaborate on this proposal.

It's really looking to see whether engaged communities that are quite diverse, that come from different kinds of groups, some are located in institutions, academic institutions, others are grassroots patient organizations, others are established registries, others are foundations.

It is to see if these PPRN communities can work together to achieve an evidence generation project in a way that has not been done before. I think one of the keys is also the idea that people that have raised their hands to say they were

interested in being engaged in research, whether we can actually come through with that and see how quickly they can recruit folks to this trial for this question.

DR. NORQUIST: Other questions? Leah?

MS. HOLE-MARSHALL: Thank you for that great introduction. Along the same lines related to our lessons learned for PCORNet in general, we know that the outcome of the study will be a report that at least gets logged, but will the lessons learned -- is there a plan for a specific report or document that will help us understand what we did or didn't find?

DR. FLEURENCE: All the PCORNet demonstration projects have an evaluation time included in them to sort of assess as they go along what the barriers are, what the lessons are, what the learnings are, so that will be integrated into the work the study investigators need to do, sort of at the same time they are actually conducting the study.

MS. HOLE-MARSHALL: That results in kind of

a final report about that, a summary?

DR. FLEURENCE: Yes, they also have interim reports as well that will be available.

MS. HOLE-MARSHALL: Generally speaking, we don't see those and those aren't published, the interim reports. I know there are progress reports that are due under any of the contracts, but those are more for internal monitoring, as I understand it, related to the contracts.

DR. FLEURENCE: That PCORNet demonstration projects, we do have an evaluation milestone, which I believe is different from our regular PCORI projects. These can be made available to the Board, certainly.

MS. HOLE-MARSHALL: The question I think I have is because we are trying to learn from it, is there a dissemination plan even to the other PPRNs, for instance, or CDRNs that are participating, to say here is what we learned from it, and here are the changes that we are recommending, or no changes?

DR. FLEURENCE: More informally every month at the PCORNet Council meetings, there are standing

items on our current demonstration projects, and as the PPRN demonstration projects kick off, we think early summer, they will join the standing item where the lessons and challenges get discussed at the PCORNet Council level.

MS. HOLE-MARSHALL: We may want to think about a library that is in addition to our open door so researchers that are not involved specifically in the PPRN but are trying to access it would also be able to benefit from these lessons learned.

DR. FLEURENCE: Yes, agree.

DR. KRUMHOLZ: I just want to say publicly that I want to commend the PPRNs, really people powered research networks, that we put together. Their willingness to work together and to try to put together a proposal that crosses groups and to try to see whether or not they can build this infrastructure and capacity to enroll patients. It is not easy to do.

The particular center that is leading this with Andy Nierenberg and his group at MGH is an exemplary center and one with a great track record

in the past. The others have come on board together.

I just want to say that I think this is a very promising move, that I know the Board has been a lot of consideration about how to continue to strengthen and position this, these PPRNs reflect the very best to the Board to be able to empower individuals to answer the questions that are most important to groups of patients, and in this case, across a wide range of conditions.

I just wanted to say publicly that this idea of going across, collaborating, trying to build stronger models that might scale, and even go beyond the funded PPRNs as they stand, is a very good move, and is much appreciated, I think, by the Board.

We know this is not easy to try this coordination, and it is nice to see it went through a study section, it went through the Selection Committee, and now is being presented to the Board for approval. I want to say I support it.

DR. NORQUIST: Okay. Allen?

DR. DOUMA: How were the people involved in

selecting the metrics for measuring well-being? The people in our PPRNs, those people that Harlan is referring to. We want to be able to show the engagement of patients and caregivers early on lead to better outcomes in the research. My question is how were they involved in making the determination of how we are measuring well-being, what metrics we are using.

DR. NORQUIST: The engagement of the participants.

DR. FLEURENCE: Thanks, Allen. Early on, the PPRN leads met together, I believe at least a couple of times, and then started floating possible ideas around that would work for their communities, and then went back to their patient and participant communities to discuss the idea, and there was some prioritization done throughout the different PPRN communities.

When the leads came back together, I think there were three options on the table, and this ended up being the optimal study question. Certainly, the application does go into some detail

around how the different communities were engaged with the selection of the question.

DR. NORQUIST: I think he's not asking just about the question, but the measures for well-being. Standard measures, that the group agreed these were ones they were willing to use.

DR. FLEURENCE: That's correct.

DR. NORQUIST: Other questions/comments?

[No response.]

DR. NORQUIST: I need a motion to approve.

M O T I O N

DR. LEVINE: So move.

DR. NORQUIST: Thank you, Sharon. A second? We have several. Okay. We don't have to do a roll call, right, since everybody is in the room?

All those in favor, say aye, raise your hand, that would be the easiest way.

[Show of hands.]

DR. NORQUIST: All those opposed?

[No response.]

DR. NORQUIST: Anyone abstaining?

[No response.]

DR. NORQUIST: On the phone? We have the recusals, I have to point that out. Allen, you are not recused.

DR. DOUMA: I vote in favor.

DR. NORQUIST: Harlan Weisman?

DR. WEISMAN: I'm in favor.

DR. NORQUIST: Okay, thanks. Just for the record, Debra Barksdale, Steve Lipstein, Alicia Fernandez, Barbara McNeil, and Andrew Bindman were recused. Thanks. Thank you, Rachael, very much.

The next and last session before we have lunch is the report on application enhancement efforts. We have several people here. I hope we can do this in the time allotted with all the people and have room for discussion.

We have Evelyn Whitlock, who is our Chief Science Officer. Jean Slutsky, our Chief of Engagement and Dissemination, and Program Director for Communication and Dissemination Research. Regina Yan, our Chief Operating Officer, and Bob Zwolak, Chair of the Science Oversight Committee.

DR. SELBY: I just want to say first of all that I think Jean or Regina and Bob are going to do the presentation. Evelyn has been very involved in this as well.

I want to thank the SOC and its members and its subcommittees for a ton of work over the last year leading up to this and launching, I think, us in a direction that we really need to go, which is to explore every aspect of our application process up to and including merit review, and tweak those things that the research community and our own insights tell us could be improved.

MS. SLUTSKY: Good morning. Gray, this is going to make you very happy, we only have six slides, seven if you include the title slide. We have given Evelyn a break since she's presenting quite a bit today.

The application enhancement efforts began in 2015 and spanned into 2016. Just to refresh your memory, there were four work groups and committees, and we commissioned an external review. This addressed your concerns about funding announcements

through the application process all the way back to giving summary statements to applicants.

There were about 45 recommendations across the work groups and the external review, and three overarching principles came from these reports. One was to ensure PCORI culture supports applicant success, to implement change management processes across the continuum, and to improve and increase communication with our external stakeholders.

These are the broad recommendation categories. You have these in your background materials. I don't want to read through all of them, but just to let you know it really starts at the beginning and goes all the way through benchmarking our activities with other funding agencies.

I just want to talk about what we have done so far on the recommendations and then Regina is going to drill down a little bit.

We have organized an internal staff steering committee of stakeholders and decision makers across PCORI. We have categorized the

recommendations for implementation using an immediate time cycle, which is cycle three, 2016, to post-August 2016 funding announcements, and then short term, which is cycle one, 2017, to the post-February 2017 cycle.

We are also in the process of developing a request for proposal for change management processes.

MS. YAN: With the staff steering committee, we focus on a few things. One is we want to make sure that what we do will improve the applicant's experience, and also the application quality. We also want to make sure we improve the process efficiency.

We looked at all the recommendations, we prioritized them and put them into two categories, one is immediate and the other one is short term. One thing is we are trying to be very mindful that we don't respond to the concerns that we make changes so frequently by introducing more changes.

That is why we want to look very carefully and we want to make sure that what we introduce is

going to help the applicant, particularly in experience.

One thing we will be doing, we talk about immediate, for August 2016, just a couple of months from now, the commissioned study. We actually have a lot of resource material for applicants, tons of them. They are all on our Web site, but they are kind of hard to find and kind of hard to navigate.

So, one thing we do immediately is to do a complete and full review of all the resources and all the guidance materials we have, so that is something we do right away. We hope with that it will make it much easier for our applicants to find information, useful information, that will guide them and help them with the applications. Ease of use and ease to find is going to be important criteria for us.

We will also standardize all the language and templates, and occasionally we will have places where we describe things slightly differently that could be confusing to applicants, we want to pay attention to that.

We want the templates to be easy to use, and currently, with our broad PFAs, we have multiple templates. We will also be consolidating the PFAs, and they have specific sections for each particular program area.

We are also going to start planning our change management process. So, this is for August, just a few months from now.

When we talk about short term, we are really talking about Cycle 1 2017, that will be the PFAs that will be posted in February 2017.

These are the items that we think will take just a little bit longer to do, but we can do it by February. One is the short term, research plan templates. I know there is a lot of talk about that.

We also want to review our PFA cycle time lines. We know a lot of applicants would like to have more time. We are looking to do a lot more work in the pre-announcements, targeted promotion of our PFAs.

For the research plan template, it required

us to really make adjustments in our system to build that template, and we also want to include our reviewers and our applicants in testing our system, so they can give us feedback as to whether this is an online system that is very easy to use, intuitive, and does not have a lot of duplications.

By February, we will implement our change management process, so any time we want to introduce a change, we want to make sure it has gone through a very thoughtful review, that the changes will not cause further burden or unnecessary burden or confusion to applicants.

These are the main things we have.

Next steps, we will continue to work through SOC as we make progress, we will report back to SOC on the status on a regular basis, and also provide you with additional details in the future.

DR. NORQUIST: Bob?

DR. ZWOLAK: From my perspective, I think that PCORI is responding to our customers. I think we heard pretty loud and clear that there were concerns about our process and at a variety of

levels. We have opened the gates and gotten lots of feedback, including a formal consultant, and I'm impressed the staff has a very cogent and timely plan to respond.

I think we are going in the right direction. We have heard negative feedback comparing PCORI's phone system to the IRS where you never speak to the same person when you call, we have heard, I think, newer and better positive feedback.

One of my colleagues in Texas said PCORI used to be his worse favorite granting agency, and has now flipped to his very favorite because of the communication with staff that he gets and the appropriate channel feedback that he receives.

So, I think this is a process that at least to this point is working well, and I'm impressed that we will implement changes in the very near future.

DR. NORQUIST: Sharon?

DR. LEVINE: Is this the right group to look at incorporating Harlan's suggestion for a

checklist to be incorporated in the application about the methodology standards?

MS. SLUTSKY: Yes, it could be. One of the things we will be looking at is the application template itself, and the desire that right now it is very complicated. Also, the IT system behind it doesn't allow similar parts of the application to be populated with the same information, so if you are prompted to enter something --

[Whereupon, at 11:48 a.m. the audio feed to the Webcast was disconnected and a luncheon recess was taken.]

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

[1:01 p.m.]

DR. NORQUIST: Wow, it's so silent. I want to welcome everyone back. We are now going to move to our next agenda item. This panel that we have next is our Stakeholder Panel, Specialty Physicians, of which there are several of us actually on the Board. This panel is a third of what is now a regular feature of our Board meeting.

Today's panel features specialty physicians. The Board looks forward to hearing from them, and I'm going to let Bob Zwolak, who is moderating this panel, to introduce our guests. Bob?

DR. ZWOLAK: Thanks very much, Gray. I'm extremely pleased to moderate this afternoon's initial event, which is the Stakeholder Panel with representatives from medical specialty societies.

For those who may be less familiar with these specialty societies, the mission statements typically include enhancement of clinical care, education, research, and advocacy for patients and

providers. The professional societies thus far have engaged to a variable extent with PCORI.

You heard earlier this morning in the proceedings about constructive interactions with radiology and nephrology societies with PCORI, and we are anxious this afternoon to hear the comments of our guests regarding their perception of PCORI, now that we just passed our sixth birthday.

We have invited representatives with different backgrounds and different specialties. Dr. Christopher Cox, Dr. Neil Kirschner, and Dr. Richard Schilsky have been kind enough to agree to visit and offer their thoughts this afternoon. Their bio's are in our agenda. In brief, these three individuals have made substantial contributions in their field and to medicine as a whole.

Dr. Cox is an Associate Professor of Medicine and Clinical Faculty in Palliative Care at Duke. He directs the Duke Prosper Program and he co-directs the Medical Intensive Care Unit there. Dr. Cox has been active with the American Thoracic

Society. He is a multiply published investigative author, and he is PI on a PCORI funded grant.

His research involves understanding and improving the critical care experience of patients and their families, which is terribly important. I know we will be anxious to hear his global thoughts and also perhaps some details of his personal experience with PCORI's application process.

Dr. Kirschner is a Senior Associate in Health Policy and Regulatory Affairs at the American College of Physicians. Dr. Kirschner manages Affairs at the Epicenter of Patient-Centeredness, which is the medical home and indeed the medical neighborhood.

Dr. Kirschner served for many years as a clinical psychologist in Baltimore before moving a bit south to Washington where he was a member of the professional staff of the Senate Joint Economic Committee and House Ways and Means Subcommittee.

Thereafter, he joined ACP where he focuses on multiple issues and interfaced with PCORI, including the patient-centered medical home

comparative effectiveness and prescription drug abuse. I'm sure Dr. Kirschner will bring some interesting observations to PCORI today.

Third in our panel is Dr. Richard Schilsky, an internist and medical oncologist who is Senior Vice President and Chief Medical Officer of the American Society of Clinical Oncology or ASCO, a previous president of ASCO. ASCO is the largest professional organization representing physicians who care for patients with cancer.

Dr. Schilsky has held a substantial number of roles during his career with a central theme being focused on clinical leadership. Dr. Schilsky chaired the NCI sponsored cancer and leukemia group B for many years, and he served in a wide range of other roles at NCI. He has also served on advisory panels of the FDA. He is a member of the Board of Directors of Friends of Cancer Research. Dr. Schilsky is certainly in an unique position to offer observations about PCORI.

Without further ado, I'd like our guests to offer their comments. We have asked each of them to

speak for 10 to 14 minutes, and after they finish, we should have sufficient time for Q&A. We would certainly love to hear kudos about PCORI, it may be more constructive to hear your unvarnished critiques regarding how PCORI is meeting our mission from your perspectives, what you perceive as our gaps, and any specific suggestions you might have for improvement.

Thank you. Dr. Cox?

DR. COX: Again, thank you all so much for letting me come here. I'll try to speak not just on behalf of ATS, but I'm also a pulmonary doc, and certainly I can't thank you all enough for also giving me personally some PCORI funding. Again, fabulous. We are very excited about the project.

I know a lot of folks here probably understand the immense burden that folks with pulmonary and critical illnesses, pulmonary diseases and critical illness, shoulder both in America and globally.

Our group, ATS, thoughts from some of the leadership was perhaps this perception of perhaps being relatively overfunded in comparison to a

number of other organ systems and what not. I won't mention the gentleman sitting right beside me.

They felt it was really important that we emphasize that right now the folks in the ATS, the American Thoracic Society -- there is great enthusiasm for taking on this type of research. We feel like we can make a really large difference because of the readiness of our field for effectiveness and implementation research.

Just a quick word about the ATS. It is not just doc's. We have a substantial portion of nurses who are members of our organization. There is probably about 10,000 plus clinicians in the U.S. across every state.

I thought what I could do was just briefly touch on some general topics of interest to the group, and then get a little bit more specific. We had a couple of nice calls with leadership of different assemblies within ATS yesterday, and they kind of voiced their thoughts.

The ATS is very supportive of comparative effectiveness research. We also feel that right now

what we are hearing a lot from community docs is a great interest in trying to translate science into practice at the community level. This is something we are all aware of.

We are all aware of our shortcomings, perhaps you all have heard there is a famous critical care study where they actually inflated people's lungs a little less than we had been for a number of years, and that was associated with a remarkable gain in terms of lives saved, yet still years later we are unable to show this has been taken up in the community very effectively. This is just one example of many.

We are very interested in pragmatic clinical trials. There is a lot of excitement for this in the scientific meetings we go to. In terms of topical areas, there are three things I was told to speak about.

The first is the idea of studies that are this intersection of palliative care with severe pulmonary disease and critical care. A lot of doc's, a lot of clinicians, they keep asking us how

do you help doc's and nurses communicate better with families and help them make decisions as partners.

Also, there is a lot of interest in diseases that may be less common but are quite resource intensive. For instance, pulmonary hypertension and interspatial lung disease.

Some very specific topics now, there is a lot of excitement testing high flow oxygen delivery devices versus non-invasive ventilation in acute respiratory failure, and evaluating in a systematic way EHR embedded tools such as early warning detection systems, which of course in our hospitals nationwide is the causal death of about 50 percent of those who do die in hospitals.

Last, just a suggestion for discussion. I'm not exactly sure how this fits in with the mission. There is concern over outcomes measures, actually. We struggle with this. A lot of what we do focuses on restlessness, pain, things of this nature, depression, anxiety, and PTSD. There is just a lot of concern right now. We are not sure what are the best metrics for this in our

population. It's hard to get psych metric research funded.

That is kind of in the landscape here, but that was one of the things that a number of our members felt were on their plate right now.

I wanted to just give a very quick overview, and we would be happy to discuss more maybe after these gentlemen make their statements.

DR. ZWOLAK: Thank you very much. We should probably hold questions until the end. Dr. Kirschner?

DR. KIRSCHNER: Hi there. I want to thank the PCORI Board and leadership for inviting the American College of Physicians to be here.

You can't see it, but they have our pictures right in front of us, it's a little intimidating sitting here with these gigantic pictures.

[Laughter.]

DR. KIRSCHNER: Consistent with the principle of transparency, which is throughout PCORI, I must admit that I am a proxy today for Dr.

Steve Weinberger, our Chief Executive Officer, was supposed to be here but he's caught 10 blocks down here running a major policy meeting, and I'm sure he would do a much better job than I would do, but I will try to uphold the name of the College, and those issues that I am not familiar with, I will clearly link up with as we discuss with the powers that be.

The one quote that he asked me to say is that he has always found PCORI to be very open and engaging with physician communities' input and suggestions. You should be aware of that.

A little bit about the American College of Physicians. The American College of Physicians is the largest medical specialty organization. It has 143,000 physicians and students in internal medicine. Our members practice primary care as well as the internal medicine subspecialties, such as cardiology, oncology, and so on.

The College has a long history of interest in comparative effectiveness research beginning in the 1980s with a clinical efficacy assessment

program. It began looking at what was called something that looked like comparative effectiveness research at that time, and started looking at clinical practice guidelines to be used by its members and the medical community.

Its journal, the Annals of Internal Medicine, is an internationally renown disseminator of comparative effectiveness research, with Dr. Sachs who was the editor of that journal for a number of years.

In 2008, the College made a major policy paper concerning comparative effectiveness research. Think of the context in 2008, what was happening in Congress, particularly related to this particular institute. In this policy paper, I will quote, "The College supported the establishment of an adequately funded independent entity to sponsor or produce trusted research on the comparative effectiveness of health care services."

Based on that policy position, we testified at a number of congressional hearings, and we are very proud to think we had some small part in

advancing the enacted legislation that led to the establishment of PCORI.

One thing you should know is from the very beginning the College emphasized the importance of both clinical effectiveness research and cost effectiveness research. We still think that is an important part of a portfolio like PCORI, even though we know that the legislation takes it out of your purview. We think it is very important for stakeholders to have that type of information.

Cost effective information and clinical effectiveness information is the foundation for many things that the College is engaged in. Today, we have a very valued care initiative, spend a lot of time and resources, that provides toolkits and resources for our members and the medical community on how to provide high quality cost effective care. Our involvement in the American Board of Internal Medicine's Choosing Wisely program is based on the foundation of comparative effectiveness research.

ACP is actively engaged in PCORI. Our members serve on the Board, various committees and

panels. They participate in multiple work groups and workshops. We provide comments to you when you send out requests for information. We also have been involved in some research projects that have been funded through PCORI. I'd like to share with you a couple of these that are of interest to me anyway.

One is an engagement award that we did as a collaborative with our fellow primary care organizations, so the family physicians, the osteopath's, the pediatricians. It looked at how do our members view comparative effectiveness research. In summary what we found is while the term "comparative effectiveness research" may not have been well understood by a number of our members, particularly the older members, the activities involved were clearly understood, favored and engaged in, such things as comparing the role of effectiveness in the various ways of treating a particular medical condition, looking at using that information for practice guidelines, looking at using that information for shared decision making

with patients. This is something that all the members favored and supported and engaged in.

The other thing that we found was that in each of the organizations, the preferred way of getting this information was through their organizations, so for the family physicians, the American Academy of Family Physicians, ACP for the internal medicine folks. That preference, and where that preference comes from is perhaps more trusted, they have easy access.

I think there is a message for PCORI, that in terms of your dissemination, you should keep these organizations close and use them as much as you can to get this information out into practice.

That was one study. The College engaged in an advisory capacity in two other studies that I will align with the College's interests, and I believe we provide a lot of services.

One is a project called Project Care Align. I don't know if you are familiar with it. It is attempting to change the perspective of medicine, getting away from treating per se the medical

condition, lowering Hemoglobin C or lowering blood pressure, to focusing on the health issues that are important to the patient.

What might be important to the patient might be something along the lines of walking my grandchild to preschool every day without getting dizzy, and working on my medical condition should take that as a priority in terms of how it is cared for.

Another one that has been as an example that I like very much is it is important to me to have a glass of red wine with every dinner. Well, if you're going to treat me and treat my medical condition, take that into account.

That is one of the projects, and they are already engaged in implementing this up in Connecticut as part of the study. Mary Tinetti at Yale and Caroline Blaum from NYU are involved in that project.

A second project very aligned with the College's interests has to do with care coordination and transition. Mark Williams at the University of

Kentucky has a project, Achieve, funded through PCORI, looking at what transition approaches are most effective and most important and preferred by the patient. The College has been very much involved in providing advice to that particular project.

The College is a membership organization, and as such, it controls what our strengths are in terms of how we are best engaged with PCORI. The College and its membership are most helpful, I think, in terms of PCORI, in terms of providing advice, providing feedback, providing comments. I think we are very well aligned to do that.

The second thing is dissemination, and I mentioned that before. I think we can really help PCORI get the information out, and I also believe we can serve as an environment where PCORI can deal with a very important issue in terms of trying to find the best ways of getting the information out. We offer a sort of research environment where we can get into our many members' practices and look at ways in which things they hear, they are actually

engaged in. I think that is an important element I feel you folks should look into.

The last thing that we do very well is take information provided by PCORI and other entities and put them into clinical practice guidelines to be followed by our members and the medical community in general.

As an organization, we are proud to be associated with PCORI. We are pleased with the progress the institute has made in fulfilling its mission up to now, and we look forward to continuing success in providing important information to all stakeholders in the future.

There are some areas that I hear from our staff and our members that we need to sort of look at. Your funding approach. Apparently, there are a number of funding streams within PCORI, and our membership reports at times that it is hard to figure out which funding stream is most appropriate for which type of research.

We would recommend that you perhaps look at that issue. Once the appropriate funding stream is

clear, we have heard from some of our membership that they feel you could streamline the actual application for the funding experience. I think you would get more engagement of the physician community doing that.

We heard you have an ambassador program, and apparently the ambassador program works really well for those projects that are directly being funded. ACP advises basically, we are partners in an advisory capacity.

Our ambassador happens to be the head of our Center of Patient Engagement. She has a lot of knowledge and information that I think would be of help to PCORI, but her feeling is her involvement up to this point, and this is a quote, "Has been relatively meaningless," and we would encourage that for the various ambassadors, more emphasis be made in terms of their engagement.

I heard feedback in terms of when information or advice has been given, it's been accepted very well, but we think more can be done in terms of sending feedback back to the feedbacker in

terms of how useful the information was, what has happened to it, what has been the effect of that information.

I think I've said my 12 minutes of comments, and I will pass it on to our next speaker.

DR. ZWOLAK: Thank you very much. That was terrific. Dr. Schilsky?

DR. SCHILSKY: Thanks so much. Like my colleagues here, I want to thank you for the invitation to come and meet with you today, and also start with a bit of an apology, which is just to say that I was out of the country all week last week, so I really didn't have an opportunity to prepare as much for this meeting as I might have, I didn't get home until late last night. I have prepared remarks, but I am going to offer some perhaps random reflections, hopefully still somewhat coherent after the long travel day yesterday.

I have noticed, of course, and Dr. Cox has alluded to the fact that a large proportion, maybe now the largest proportion of PCORI funding, is going to support cancer research. I think that is

largely a reflection of several things.

One, of course, is the continuing unmet medical needs that many cancer patients have, but also it is a reflection of a much greater opportunity now than ever before to actually conduct comparative effectiveness research in cancer because there are in fact more treatment options, more choices, and more things that can be compared than ever before, when there were few or no choices for how to treat a patient with a particular type of cancer.

There really wasn't much need for a comparative effectiveness research. It was really more about discovery research and clinical effectiveness research, bringing new treatments forward.

Now for most every kind of cancer, we have not only one but multiple therapy options in each line of therapy, and in fact, when you add to that the enormous cost of many cancer treatments these days, guiding patients through a discussion about what is the best possible treatment option for them,

given their clinical status, their preferences, their goals, and their financial resources, is more important than ever before.

Having data available to oncologists from comparative effectiveness research studies can really be valuable in helping to guide those discussions.

Like ACP, I'm sure ATS and ASCO produces clinical practice guidelines, we have been in the guideline business for 20 some years. Our guidelines sort of are known for going deep but not broad, so we have guidelines that are not across all types of cancer, all lines of therapy, but guidelines to try to address genuine clinical conundrums, areas of genuine uncertainty that oncologists face every day.

What we find, and what I'm sure what most guideline development organizations find, is that although we attempt to base our guidelines on high level evidence from well conducted prospective clinical trials, it is very difficult often times to get the necessary data from the literature because

it simply doesn't exist.

Even the NTCN, which produces much broader cancer guidelines than ASCO produces, acknowledges that only about 15 percent of their guideline recommendations are based on level one evidence from the medical literature.

There are huge gaps in our knowledge that we simply can't fill by continuing to do the traditional prospective randomized clinical trials because the trials are too expensive, they take too long to get endpoints, and in cancer these days, as I'm sure you are aware, every common cancer is now becoming a collection of rare cancers, as we continue to molecular subtype various sorts of cancer, we are now going from a very common cancer like non-small cell lung cancer to mutated non-small cell cancer, which is two percent of non-small cell lung cancer, or loss mutated non-small cell lung cancer, which is one percent of non-small cell lung cancer.

It is extremely difficult to do the types of prospective randomized clinical trials that have

typically been necessary to advance the field when every tumor type now becomes a type which is actually difficult to find patients for study.

Our patients now have more choice, they have longer survival, and as I mentioned, they are confronted with lots of financial concerns. ASCO in recent years has been very focused on this whole question of value in cancer care.

Last June, we published our conceptual framework for assessing the comparative value of cancer treatments, published in our journal. We will be publishing next week an update or revision to that, which reflects comments we have received on the first version of the framework that was published last June.

Among the comments that we received, including comments prominently from patients, was the fact that the framework, which is based upon sort of common clinical measures of clinical benefit, toxicity, improvements in quality of life and so on, doesn't contain enough patient-centric outcomes in the value framework.

We agree that it does not contain that, and it is not because we are not interested in it and wouldn't like to sort of use patient-centric outcome measures to help frame the value discussion. It is really because there is still in the cancer clinical trials literature relatively few patient reported outcomes that are captured or reported.

Our value framework is really based on an analysis of published clinical trial data. If it is not part of the clinical trial publications, whether it is collected or not, we have no access to it, and we can't build it into the value framework proposition.

Certainly, my hope is that as cancer researchers and clinical trialists and product developers continue to bring forward new advances in cancer treatment, that they will be able to incorporate more patient reported outcomes that will rely in part on groups like PCORI to work with our community to develop the appropriate outcome measures that really reflect what is important to patients.

You have already heard this from Dr. Kirschner, the issue of dissemination. Of course, ASCO has many dissemination vehicles. We have multiple journals. We have multiple Web sites. We have many meetings. Our big annual meeting is coming up in about 10 days from now. We will have roughly 40,000 people in the convention center in Chicago to hear what's new and what is happening in cancer.

We still have evidence that even things that are known to be highly effective in cancer treatment are still not well disseminated into practice.

We saw a publication recently in our journals suggesting that there are great disparities in the prescribing of Herceptin to women with HER2 positive breast cancer, even though Herceptin is the most effective treatment that has been developed for HER2 positive breast cancer. In many cases, there are women, typically minority women, who are not getting access to that treatment.

This year, we will have an abstract at the

meeting showing that for women who are BRCA1 carriers, whether or not they are offered so-called risk reducing surgery, prophylactic mastectomy, and so on, is dependent to some extent it seems on racial and ethnic considerations.

A study of a report or analysis of a large registry essentially showed that African American women were less likely to be offered risk sparing surgeries than either white or Hispanic women. A very important red flag that we need to understand and pay attention to.

Again, it emphasizes the need for disseminating what is known to be effective into all segments of our community, and that is clearly an area of high interest to PCORI, but I think again deeper engagement with the medical professional societies, hopefully, we have mechanisms to reach our constituencies, our communities, our patient populations, that can supplement and build upon and enhance what PCORI also has available.

We can also determine the extent to which the desired best practices are actually being

incorporated into clinical practice. ASCO has had for many years a quality improvement program that we call "QOPI," the quality oncology practice initiative, which is an oncology self assessment program where we publish quality measures based on our guidelines and other evidence in the medical literature.

Those measures are used by oncology practices to assess their performance against those measures. We send them twice a year a report card on how they are doing in meeting the quality measures, and we can incorporate into our quality measure development things like the recommendations from the Choosing Wisely campaign, which we also participate in, or recommendations for new research findings that might be disseminated through PCORI research that we believe should be a change in medical practice, and we can determine whether in fact medical practice is changing in the desired direction.

We are building now what we consider to be a major defining initiative probably for the next

decade, an attempt to develop a rapid learning system for oncology that we call CancerLinQ. It is an acronym that stands for Learning Intelligence Network for Quality.

CancerLinQ is basically an initiative to collect the complete electronic medical record from every cancer patient in every practice in America that wishes to participate in the program.

CancerLinQ is being deployed right now. There are medical records being collected as we speak from all around 30 or so vanguard practices around the country. We will announce at our meeting probably that roughly a million patient medical records or medical records of roughly a million patients have already been collected in the CancerLinQ platform.

The goal is to over time make that many millions of records and to follow up on those patients prospectively and longitudinally.

CancerLinQ will itself become an important vehicle for doing comparative effectiveness research based on real world data. We will be able to use

CancerLinQ as a platform for doing registry-based clinical trials.

We will be able to use CancerLinQ as a mechanism to identify cohorts of individuals with similar characteristics who receive different treatments and monitor their outcomes. We will be able to look at outcomes of patients who are not customarily included in cancer clinical trials, like older patients, like patients with significant organ dysfunction or other comorbidities.

We are very optimistic about the impact it may have on our profession over time.

I don't have a lot of recommendations to offer, but I will make a few comments. I still think that to a great extent PCORI is a fairly well kept secret, rather unknown in the broader oncology community.

I looked this morning on the Web site at the portfolio of some of the cancer related projects that are being funded. They are wonderful projects. I wonder if perhaps some of the reason that PCORI is not getting the attention perhaps that it deserves

is that many of the projects that are being funded are related to issues of patient assessment, patient surveillance, follow up strategies, supportive care measures, all of which are important, but what tends to get the attention of most medical oncologists are studies that relate specifically to cancer treatment. I think there are still relatively few of those in the portfolio. Hopefully, there will be more as time goes by.

I think the issue of having to navigate the PCORI Web site -- by the way, I want to compliment the team that put that together, I thought it was remarkably clear where the goals are very well laid out, and the priorities are very well laid out, the process is well laid out.

The PCORI parlance and how you describe your grant portfolio and the types of applications you have and so forth was unique and sufficiently different from typical NIH terminology that I think many people still find a bit confusing, and the comment was made about people not quite understanding which funding mechanism is appropriate

for which kind of research, and I think you need some greater clarity around that, and that would be important.

One specific thing I wanted to offer just based on my own experience in the last few years at ASCO, we get a lot of requests from PCORI applicants to provide letters of support for their applications.

Most of them end up on my desk. The request is typically something along the lines of my colleagues and I are writing a PCORI application with the following title, as ASCO is an important stakeholder group for this application, we would love to receive a letter of support from ASCO to include with our application.

I get a lot of those letters. We never just spontaneously dash off some letter of support. My view at least is that if ASCO is actually going to endorse an application in some way by writing a letter, we need to actually understand what the application is about, whether we believe it is meritorious, understand what its potential impact

could be, and perhaps most importantly, I like to insist that the applicants that actually explain to me what in their minds it means when they say ASCO is an important stakeholder.

Of course, if it's related to cancer, we are a "stakeholder." We represent all the oncologists in the country and more importantly, their patients.

Almost anything that has the potential to improve the outcomes for cancer patients, we might have a stake in. In order for us to submit a letter in support of an application, I like to have some understanding from the applicants of what exactly do they want us to do in support of their application other than be on a periodic conference call with 25 other people that they have persuaded to be stakeholders.

I don't want to prolong this. The usual response is well, you know, if we publish anything, we would like it to be presented at the ASCO meeting. My response is great, we have a whole process for that. You can write an abstract, it

will go through our process. If it is selected for the meeting, we will be delighted to have you present it. What exactly do you want for us to say we are a stakeholder in your research.

On some occasions, I am actually successful in working with the applicant hopefully to actually offer some support from ASCO that we believe will be meaningful, that will actually help to recruit doctors or patients to participate in a study or to engage in more meaningful ways in disseminating their results.

I will tell you there is one thing that you can do that would help me out, to try to be clear with our applicants about if you are asking them to provide documentation that there is engagement by the stakeholder community, to be clear what kind of documentation of that you are looking for, more so than just some cursory letter.

DR. KRUMHOLZ: Can I ask a point of clarification. This is really useful, that is why we wanted you guys here. Can you just tell us what happened? You keep going around it. I don't know

quite what you are saying.

DR. SCHILSKY: That is what typically happens. We are writing an application, it is due next week, we would love to have a letter of support from ASCO, here is the title of the application, here is the investigators, can't wait to get your letter.

I'm sure you have all been there. Sometimes we get an abstract of what the actual grant application will be. Occasionally, and usually if I ask for it, we will get specific objectives. It is a far less than optimal process.

DR. KRUMHOLZ: I don't understand. You are saying PCORI is coming to you?

DR. SCHILSKY: No, no, the applicants.

DR. KRUMHOLZ: Why aren't you telling them no?

DR. SCHILSKY: Well, because in most cases, we do tell them no. In some cases --

DR. KRUMHOLZ: Are you saying we should be telling them to reach out --

DR. SCHILSKY: No, what I'm asking, and

sorry if I'm unclear --

DR. KRUMHOLZ: I'm sorry to interrupt, I just want to make sure I understand what it is you are asking.

DR. SCHILSKY: For the applicants in many cases are under the impression, which I assume is accurate, that they are asked to provide some sort of documentation with their applications of stakeholder engagement, broadly speaking.

This is what I'm asking you to clarify because I think the applicants are unclear on what you, PCORI, are asking them to provide as documentation of stakeholder engagement.

They think if they get a letter from a medical professional society that represents that group of doctors or patients, that represents stakeholder engagement. What I am saying is when they come to me with that, I push back on that. I say if you want genuine stakeholder engagement, you need to engage us earlier, you need to think about the many ways we could possibly help to advance your project.

DR. KRUMHOLZ: We should make you an honorary member.

[Laughter.]

DR. SCHILSKY: Don't come to us at the last minute. In many cases, we don't provide these letters. When we do, we do it because we believe we can be genuinely helpful to the applicants. That is my key point, and why I think some greater clarity in communicating to the applicants what you would like to see as documentation of stakeholder engagement would be very helpful.

I think I'll stop there, but I'd be delighted to have some further dialogue.

DR. NORQUIST: Since we have started into the discussion, why don't we open it up, Bob, unless you want to make some final comments.

DR. ZWOLAK: I want to thank you. I think we could probably spend the next three hours with a Q&A session. I think we have about 20 or 25 minutes.

DR. NORQUIST: Yes, we have actually about 15 or so. Why don't we open it up for Board

comments. I think the last point, we would certainly hope that is not what we mean by "engagement," just simply getting a letter from you, and certainly we hope it comes out in the review about what is it really, how much of an engagement is this. That would not be satisfactory just to have a letter.

Dr. Kirschner?

DR. KIRSCHNER: I just want to join in the comments about the letter of engagement and to clarify what is actually being asked for, and what you expect. We ran into the same problem. We get a number of people who write and say we want you to be on an advisory panel or something, to somehow support this research. It is difficult to deal with.

DR. NORQUIST: Maybe I will put Jean Slutsky on the spot here. Jean, since you are our Chief Engagement Officer, you may want to say something.

MS. SLUTSKY: First of all, generally those applicants that do that don't fare very well in

merit review. We actually have review criteria that speaks to how the applicant describes their engaged partners and we have a lot of supporting materials to guide them through on developing an engagement plan, models of engagement.

I will say that our merit review panels are pretty astute at seeing through letters of support as being just what they are, usually they are written by the applicant for the organization, and we have all been there, right, either on one side or the other, as funders or applicants.

Rest assured that when you get those requests, you are probably not tying your ship to the most successful applicant. You are exactly right, you should be dubious about those types of requests.

DR. NORQUIST: One thing that may be helpful to save you time of even writing the letters or responding is when they come up and say PCORI has these certain requirements, I don't think you have met those, you need to go back and look at their site, and in working with them, we can help them,

and maybe get some of these letters to not even show up on your desk, and save you some time.

MS. SLUTSKY: On the funding opportunity page on the left side, it is all listed out, all the resources for successful engagement.

DR. NORQUIST: Leah?

MS. HOLE-MARSHALL: For Jean, do we have examples included in those tools?

MS. SLUTSKY: We actually have sample engagement plans. We want people to be successful with engagement. What we don't want is exactly what you described.

DR. NORQUIST: Larry?

MR. BECKER: What I think I heard is two really important things. The first one was that we need to do a better job of once gaining input from each of you, feed back on that input, where did it go, what did it mean, what did it entail or create.

The related point I think I heard was okay, now that we have some results or as results start to come, you are each uniquely positioned to be able to take that and translate that to your organizations,

your patients, your clinicians, your letter, in order to make sure that gets implemented in an effective way.

I think it is incumbent upon us to figure out how do we fix the first, how do we engineer the second, and what can we do as partners so that it is easy for you when those things come.

DR. NORQUIST: Barbara?

DR. McNEIL: Thank you very much. I have one question for Dr. Schilsky. You mentioned a number of PCORI applications dealt with oncology, and that is totally understandable. This is a request for you that I think would benefit a lot of potential applicants.

It strikes me a lot of the comparative effectiveness studies that might be done in oncology relates to pharmaceutical therapy. The sample sizes there, given that the patient populations are getting smaller and smaller, and genetic mutations are getting larger and larger.

It would be very nice and helpful to investigators if you could use ASCO's power to get

Medicare data released in a more timely fashion, and Part D data released in a more timely fashion. Otherwise, there are not going to be any real data that are robust enough to answer some of the critical comparative effectiveness questions that need answered, right?

DR. SCHILSKY: I couldn't agree more, but we will go you one better because in short order we will have CancerLinQ data, which is far more granular than the claims data that is available from Medicare.

In fact, all of that data collectively, where CancerLinQ will actually have the medical record on patients for whom Medicare has the claims data and so on, and we had multiple conversations already at NCI with the SEAL program about how we can begin to align these programs.

Peer data, as you may know, is largely based on hospital admission data. CancerLinQ data will be based largely on outpatient, and the opportunity will be very complimentary.

I take the point. We can certainly talk to

our colleagues about making this Medicare data available in a more timely fashion, but I think over time, we will be able to do it better than that.

DR. NORQUIST: Alicia?

DR. FERNANDEZ: Thank you. That was really interesting and I think very helpful for us as we think about moving forward. I have a couple of questions, and don't want to put anyone on the spot, but let me do that. This notion that I happen to agree with that PCORI is a little bit of a well kept secret among many of our specialist colleagues. I'm a primary care internist.

What do you think, and perhaps you can address this issue of what could we do differently to encourage particularly clinical trials in oncology and medicine subspecialties?

There is another well kept secret, it is called PCORNet. I was wondering if you had heard of it, and also whether there had been any discussions about any way it can link or not link or whether that had come up at all, and please don't feel shy about saying no.

DR. SCHILSKY: I know time is short. Yes, I've heard of PCORNet. I must say I don't really have a good sense of where it is in its development, what it does, how it operates, what its focus is, things of that sort.

We certainly have had discussions internally at ASCO, and I think probably indirectly with Joe, about the opportunities going forward to somehow develop relationships between PCORNet and CancerLinQ, but as both are very much in development, I think we haven't gotten very far in envisioning what those relationships might look like.

With respect to what can PCORI do to make itself better known in the oncology community, I'd like to spend a little more time thinking about that. ASCO and I'm sure the other professional societies represented here are friends of PCORI. We want PCORI to be successful. We see great opportunity for PCORI.

I think the more that we can do to help PCORI become better known and more visible and more

easily navigable to our own constituencies, we would be happy to do it.

DR. NORQUIST: Why don't we go to the other two and get your feedback. I think one of you said what is really key is the importance of involving the organization. Dr. Cox and then Dr. Kirschner.

DR. COX: I think something that might be really effective is something Dr. Selby has done some with JAMA and the New England Journal, but positioning a very explicit statement in our key journals. I think that is a great way to reach out to the research community, at least the American Thoracic Society, and a lot of eyes see that sort of thing. I think that might be the most effective to be honest, and a pretty simple thing to do.

DR. FERNANDEZ: My specialty colleagues don't actually read -- they read their specialty journal.

DR. KIRSCHNER: I agree with the statement the Chair said, it all goes to knowing what is happening within the association and seeing how PCORI can get involved. For example, two weeks we

had a meeting of our Council of Subspecialty Society. These are all the internal medicine subspecialties, representatives from each one of them, 25 different societies.

It has been going on twice a year, it's been going on with the entire engagement of PCORI, never had a request about PCORI at the meeting. I think that would be an excellent opportunity for PCORI.

There are probably other sources in each one of these organizations in which you can do that, but it all gets under the rubric of knowing what resources are available to you, which means reaching out to the associations and spending some time with them and seeing what they have to offer.

DR. NORQUIST: I think it is an ongoing kind of engagement. One of the things, particularly with CancerLinQ, it represents psychiatrists. I'm at the American Psychiatric Association, I've helped them. They are formulating a registry. A number of the professional organizations are forming these registries.

At some point, this opportunity to do a linkage across those and these other large infrastructures is really going to be critical because I know we surveyed a number of professional organizations before we built ours to see what the issues were, but everybody is basically getting into this business.

DR. SCHILSKY: I think you are exactly right. We have begun to reach out across sort of the oncology spectrum if you will. CancerLinQ will also be the platform that the American Society of Radiation Oncology uses as its registry, so we will have a direct linkage with them.

We are in discussions with the various surgical oncology societies, the American College of Surgeons, and whether we can create linkages to the National Cancer Database they have had in existence for many years.

I mentioned discussions we have had ongoing with SEAR, whether or not the data that SEAR collects could actually flow to them through CancerLinQ as CancerLinQ continues to be expanded

across the country and so on.

I think we would welcome opportunities for further discussion with PCORI. One of the issues for us, of course, is that if we are going to be able to capture the complete picture of the cancer patient experience, we actually need to collect information from other medical specialists because the cancer patient who develops a chemotherapy related cardiomyopathy and sees a cardiologist, we would like to get that information into our record.

The patient who develops hypothyroidism as a result of a kinase inhibitor therapy, sees an endocrinologist, we would like to get that information into CancerLinQ.

Of course, cancer, because it is not organ specific and it has the potential to affect essentially any organ in the body, we need to make these connections, and also with respect to survivorship because as cancer patients continue to live longer off treatment, and they have continuing medical problems related to their cancer diagnosis, they see other medical specialists.

They return to the care of their primary care physicians, and their complete cancer journey will never be captured in even something that we view as being as comprehensive as CancerLinQ.

So, I couldn't agree with you more.

DR. NORQUIST: I think it's a huge opportunity. The other issue that we discussed, it is also debilitative sustained based platforms, too, if we start to interlink together as well, because they are very expensive to get going. Alicia?

DR. FERNANDEZ: A follow up question, because it speaks to other discussions we are having. Could you give us a sense of how much you think this will cost, this CancerLinQ, and how you are funding it?

DR. SCHILSKY: So far, we have been actively building it for about two years now, so far we have expended about $20 million. Our initial estimate is it is going to cost around $50 million to get it up and running and populated with a sufficient number of cases to actually then be able to start to make some analyses.

Right now, it's been funded from a combination of ASCO's internal resources and private philanthropy that our Foundation has raised, but as we pointed out, we need a sustainable business model for it because it has to be able to stand on its own two feet over time as it develops.

DR. NORQUIST: Sharon?

DR. LEVINE: I guess a comment and a question. I think your observation about the fact of looking at the portfolio of cancer research we have funded is somewhat different than the oncologists typically look for, and that is intentional.

I think from the standing up of PCORI, the intent was to fund research that others were not going to be likely to do with a patient-centered focus. The perspective of the patient and outcomes that matter to patients has been a core part of this, which is probably why it is coming up against some traditional notions of what cancer research ought to be.

I think the second thing is one of the

challenges in doing head to head trials of drugs in cancer is the price of the cancer drugs. PCORI doesn't have enough money. I'm not sure Treasury has enough money to fund those kinds of trials to get the kinds of information you would love to have. That's my comment and my bias, I guess.

My question is in terms of CancerLinQ, you said a billion medical records. I'm assuming, are you building a platform to query practices where there is a research question? I'm not sure what you meant by you will have a billion medical records.

DR. SCHILSKY: I meant exactly that. We are going to practices. Once all the necessary legal contracting and business associate agreements and all that are put in place, we are uploading their complete electronic medical record system into a large data link. We're going back as far as when they implemented the MR in their practice, and then we are going prospectively to continue to follow those patients and new patients over time.

DR. LEVINE: These are the identified medical records?

DR. SCHILSKY: In fact, the records are identifiable as they are brought into our system and then the data is mapped to a common data model, aggregated, and then de-identified, and only the de-identified data can actually be accessed.

DR. LEVINE: Are you getting patient by patient approvals to do this?

DR. SCHILSKY: We have a patient opt out model. All the patients are informed that their doctor is participating in CancerLinQ, and have the opportunity to ask their record be excluded from the system. It is not an informed consent model. We actually have a determination from an IRB that CancerLinQ is not in and of itself conducting research, it doesn't require informed consent.

All the records are collected under the terms of a HIPAA compliant business associate agreement. What we do is we are performing quality analytics on the patient records and returning to the participating practices quality improvement reports, which is acceptable business practice under HIPAA and doesn't require patient informed consent.

That said, we did think it was important that patients be aware that their records are included in CancerLinQ, so we have a requirement that the practices disclose to the patients that the practice is participating in CancerLinQ, and unless the patient opts out, their record will be included in the system.

DR. NORQUIST: Joe, you get the last word.

DR. SCHILSKY: We have published all that in our journal, it is all on our Web site. We try to be very transparent about what our regulatory standards are for the system.

DR. SELBY: I think in terms of this concern that Chris first mentioned or Neil first mentioned about where do I go for what or what's really the right application process. I think that is really a point well taken. I think we can look at our Web site.

With respect to CancerLinQ, you mentioned the magic words, "common data model," and I think there should be a lot for us to talk about as we start sort of building the cancer part of the common

data model.

One question. We had a model here I think that physicians organized in societies who were writing guidelines would often sort of come to a fork in the road and for lack of evidence, as you say, would not know which way to advise their colleagues to go. They would then being aware of PCORI's presence get together and actually produce CER applications to PCORI.

It's one thing, you can see the questions to PCORI, and we welcome those, but is that a flawed model that the societies themselves would find researchers to put their proposals together, because that would sure be the opposite of getting a letter the day before an application is due saying would you like to sign on.

DR. SCHILSKY: I don't actually think it's a flawed model, and in fact, in part based on conversations that we have had over the last year or so. We are in the process right now of working with our guidelines panels to get them to identify questions where they feel in the process of

developing a guideline they believe there are significant evidence gaps that they would like to see filled in order to be able to write a more comprehensive guideline.

Now that CancerLinQ is beginning to actually accumulate sufficient amounts of data, we are then going to the CancerLinQ informatics team and saying okay, we have some high priority clinical evidence gaps, can we fill these with data that is potentially available in CancerLinQ.

Where we feel that we have the data resources to address an evidence gap, that is where we hope you will be seeing some applications from us to actually then conduct the studies to fill those evidence gaps with data that would be accessible to us in CancerLinQ.

DR. SELBY: Do you have thoughts about that?

DR. COX: I don't think it's a flawed model. I think we just need to do better ourselves kind of organizing around these issues. We have no excuse, I think, probably. We could think of stuff.

DR. KIRSCHNER: I can't say how well our guidelines people are aware of or feel engaged with PCORI enough to make use of how this model works. I think that would take some effort on my part, and it may take some exploration on your part, too, in terms of how well we understand the capability to fund.

DR. NORQUIST: I will just add, Joe, since the guidelines committee for American Psychiatric is under my council that I chair, so we have actually had exactly the same conversation. We have kind of been looking at AHRQ's evidence-based synthesis to decide on which cherries we could actually pick. I think it actually just dawned on me that here I am the chair and we haven't had these kind of conversations about where we fill the gaps.

I think it is back to this interface with the organizations about what might be possible to link with PCORI.

Thanks. Michael?

DR. LAUER: Guidelines would say something like let's say you want to figure out what dose of

aspirin to give a patient who has had a recent myocardial infarction. Of course, we don't know the answer to that.

The guideline, as a Class 1 guideline, would be enroll eligible patients into the adaptable trial. That itself would be a guideline. If you don't know what the right answer is, then the standard of care would be consider enrolling a patient into a trial that will answer that question. Something to think about.

DR. NORQUIST: Then you have to get the patients to agree to that. Thank you all very much, we really appreciate it.

[Applause.]

DR. NORQUIST: As they say, it is the beginning of a conversation, so it is not the last. Thank you.

We now move on. Jean Slutsky, Joanna Siegel, and Debra Barksdale. Debra, this is your panel on dissemination strategy. This is an area that we have had some discussion about this morning and one we want to spend some time on. I hope the

presentations are fairly brief, and then we will have time for discussion.

Debra, I'm going to let you start this off, unless one of the others are. I think this is Joanna's first time in front of the group. Jean will introduce you.

DR. BARKSDALE: Thanks. We are delighted to be able to present to you the work that is in process related to dissemination and implementation at PCORI.

The way this is going to work today is we are going to have some presentation of the background, implementation and dissemination activities and findings that PCORI is currently engaged in, and then some selected high impact studies, and then discuss the sort of groundwork that has been done.

There was an initial presentation to EDIC back in -- can you hear me? There was a presentation to the committee back in March, and then we met face to face in April and had a very productive meeting here in D.C.

With that background, I'm going to turn it over to Jean.

MS. SLUTSKY: Thank you. I'm not going to actually do a presentation, Joanna Siegel is, but I wanted to take the opportunity to introduce her. She was not able to be at the last meeting, but Joanna is on our staff and helping to develop infrastructure for the dissemination and implementation program.

I also want to point to the back that Sharon Arnold has come from AHRQ to join us for this session, and we have been working really closely with AHRQ as we develop our program both through the EDIC and at the staff level.

I'm going to turn it over to Joanna, and we look forward to a good discussion which Debra will help us moderate.

Can I just say one thing? The slides that are in your Board book are a little more comprehensive than what will be presented today.

MS. SIEGEL: Thank you. The goals of PCORI's dissemination and implementation program are

the translation, dissemination and implementation of PCORI's research findings to facilitate their uptake and to ultimately improve health outcomes.

I'd like to start with a few definitions. "Translation" is presenting the research findings in accessible language and format so that the results are comprehensible and meaningful to the intended target audience.

"Dissemination" is an active process designed to increase understanding and use of findings, and to motivate their uptake and use among the target audience.

"Implementation" is the process of integrating evidence into policy and practice.

You have all seen this language many times before, but what I'd like to highlight here is in addition to conducting comparative effectiveness research to assist patients, clinicians, and others with health decisions, PCORI is also charged with dissemination of research findings to facilitate their uptake.

AHRQ is also charged with disseminating

PCORI's findings, and with disseminating patient-centered outcomes research more broadly. For this reason, a lot of what we will be doing in dissemination and implementation will be in collaboration with AHRQ, as Jean mentioned, and I'll be talking about this a bit more later.

This slide provides a map of our program for dissemination and implementation, and shows where the activities that I'll be talking about fit in.

While PCORI's research is in progress and as some of our studies are nearing completion, we have been planning and laying some of the foundations for the dissemination program.

We have a set of activities that comprise our initial work in dissemination. These are essentially the first stages in the dissemination of PCORI's research findings, and they apply to all or almost all of our findings.

I will also be talking about our plans for dissemination of selected findings and the work we are doing now to lay groundwork for these

initiatives, most of which will occur when more of our studies have been completed, which will be the focus of much of our collaboration with AHRQ.

I'm going to touch just briefly on some of our capacity building activities. This has been underway through our engagement and science program. In engagement, the stakeholder engagement team has been convening roundtables this year with physicians, nursing, and in the future, purchaser and pharmacy benefits management organizations.

These organizations are critical intermediaries for dissemination and although dissemination isn't the only topic at these roundtables, we are discussing with these organizations their potential role in disseminating findings to their membership. The two roundtables that have taken place so far have each had more than 50 representatives of these organizations.

The engagement awards have a new emphasis on dissemination. The engagement awards for dissemination are intended to support awardees in

helping to develop processes, collaborations, and approaches to enhance their ability to disseminate PCORI research findings to their memberships.

In addition, we have a program in communication and dissemination research, CDR, as you know, which has an ongoing portfolio of awards that look at the comparative effectiveness of communication and dissemination strategies.

I'd like to turn to our initial work in dissemination for our research findings. Again, the things I'm going to be talking about here are on the immediate horizon, and are what we are going to be doing for all or most of our research findings.

As you know, PCORI's authorizing legislation specifically charges us with conducting peer review findings, both to ensure their scientific integrity and to assess their adherence to PCORI's methodologic standards.

This is really the first step in the dissemination process. It is the point of departure for assuring that the findings we disseminate are valid and trustworthy and therefore useful, and will

also, of course, provide context for the consumers of the research findings.

We are further charged with making our findings available within 90 days, with making them comprehensible to providers and to patients, and discussing specific considerations in the findings that we release.

The process for peer review and public release of findings that the Board adopted in February 2015 outline the peer review process, and it also specifies that PCORI's release of findings will be accomplished by developing and posting two 500 word abstracts, one for patients and the general public, and one for medical professionals.

This time line summarizes our process of peer review and release of findings. It begins with the primary completion date of the research, which I want to emphasize is not the end date for the contract.

It is the last point, the last date when data are collected for the primary outcome of the study. During the following interval, the awardee

completes data analysis and prepares their draft final research report, which has to be submitted to PCORI no later than 13 months from the primary completion date.

Once the draft final research report is submitted, PCORI has two months to conduct peer review and to get comments back to the awardee. The awardee then has a month and a half to respond to the comments, which PCORI can allow a bit more time if those comments are complex. Once the comments are addressed, the awardee resubmits and then PCORI accepts the draft as the final version of the research report.

At that point, the 90 day clock starts ticking, and we have three months to post the lay language abstract and the clinician abstract on PCORI.org.

Once we have the peer reviewed findings in hand, our dissemination and implementation program activities will be focusing on translation and communication of the findings. First, we will be working on developing the abstracts for posting,

which I'll talk about a little bit more in a second.

Journal publications by our investigators are another means by which our research findings will be released. We have some new activities to support public access to these publications which I will also go over just briefly.

We have the return of research results to study participants, which is an important part of our initial work in dissemination. The process for peer review and release of findings that the Board adopted a year ago February addresses this - it says "PCORI will supply awardees with a copy of the lay language abstract, and the awardee institution will make every reasonable effort to ensure that participants and partners receive this summary."

This is a role for our investigators. We do have this guidance in place, but we plan to do more shortly in the way of publicizing this provision and making sure it is on our awardees' radar.

Other early activities for dissemination will include things like investigator presentations

at conferences and meetings, conducting continuing education, which we have already started at PCORI, and the development of materials designed to communicate findings to specific target stakeholder audiences.

As far as the initial activities in translation, we are currently in the process of establishing our translation center through a PCORI contract.

The translation center's responsibilities will include the writing of the lay and clinician abstracts, and will include preparing a summary of the peer review comments for posting with the abstracts, to provide context for the findings in a format that is more accessible to readers.

The translation center will also be involved in reviewing the project summaries that are on the PCORI Web site. They will be helping to update these and put them into a more consistent format and also to improve on their readability.

The translation center will also be developing Spanish translations for the abstracts

and in some cases, translations into other languages.

In addition, for many of our findings, they will provide non-written forms for communicating to lay audiences, audio files or sometimes videos, to assist with communication to low literacy and also visually impaired audiences.

The translation center will also be involved in some of our initial dissemination activities for selected findings. These will include things like grand rounds, types of presentations, or other types of presentations featuring one or more of our investigators.

Finally, because the staff of the translation center will be immersed in reviewing all of our project summaries and also will have an early look at the draft final research reports that awardees submit, they will have a role in helping us to flag promising and potentially high impact findings.

We put out the RFP for the translation center in March, and we are actually receiving

proposals today. We expect to have a translation center up and running by the first part of July.

I mentioned earlier that we had some new measures to improve public access to PCORI research findings that are published in peer reviewed journals. We have presented this to the Board in April on the Board call, so I will just go over it briefly.

We will be requiring that PCORI awardees assure that their manuscripts are deposited in PubMed Central at the time their final version is accepted by a peer review journal. PubMed Central will make these manuscripts freely available anywhere from 6 to 12 months after the article is published depending on PubMed Central's arrangement with the journal.

Also, in order to facilitate more immediate access to findings that are published in these journals, PCORI will be covering the fees that many journals charge to provide free public access. This will include publication fees that are charged by many of the open access journals, and also fees that

other journals charge for access to a particular article.

PCORI will be paying up to $3,500 per project for articles presenting primary research findings and will also consider coverage in addition to that for large projects that report multiple findings.

This process is designed so that awardees retain discretion in choosing the most appropriate journal for presenting their findings. This policy is now up on our Web site, and we are working towards implementing it.

Another early activity that we have in place for dissemination is our limited competition dissemination and implementation awards. These awards are intended to provide an avenue for our investigators to pursue strategies for disseminating their work, and many are very interested in this. These are two year awards for a maximum of $300,000 each.

As noted, the eligibility for these awards is limited to our current awardees. Importantly,

the other major requirement for investigators to apply is they must have submitted their draft final research report to PCORI. This is an important incentive for awardees to get their research reports to us early.

We received 19 letters of intent for the first cycle of the limited competition D&I awards, and proposals for the cycle are due in June. We anticipate start dates for funded projects beginning in January 2017. This award is going to be available during three funding cycles per year, so we have actually already received some letters of intent for the second round.

At this point, I'd like to turn to our plans for dissemination and implementation activities for selected studies, those that we feel have particular potential for having a high impact on health care and health outcomes.

DR. BARKSDALE: I see a couple of tents. Harlan, do you have a specific question or comment about the first section?

DR. KRUMHOLZ: I am happy to wait or I can

weigh in now. I see a problem brewing in the way in which we are approaching this, that I at least want to surface, which is also alluded to by your last sentence.

Are we funding highly consequential work that has the potential to influence practice that needs to urgently be disseminated so people can act on it, or are we funding work that people can deliberate on for 13 months, they can take their time. It comes to us, we circulate it around, and it gets out around 15 months after the last data element was collected.

The typical thing in academics and the problem is if we report, and Mike Lauer and I both know this well, if we do report the results, of which we note that within two years two-thirds of academic doing experiments on people don't report, and if we publish, what we do is we take our time years past or 13 months past, we are not poised when the final data point is in to move acceptance in a few cases where we see sometimes with trials and quickly published, we often take our time, and then

when we publish, we rush.

Now we have to disseminate. Why isn't anyone doing anything? They have to act on our studies, you have to listen, and yet there was a big piece in the middle where we just were leisurely moving along if we did even complete the task.

The question for PCORI is are we going to do things differently. The Board adopted this, so in all fairness, the Board adopted this, but I'm just raising it as you are saying, this dichotomy on the one hand saying our work that we funded is going to move, and then your last sentence was now for the studies that we think really should move forward, and then that raises this question about the others.

It also raises the question why aren't we teaching people, including me and any other researcher, to jump on that last day, already written the analytic programs, have been ready to just turn the switch, have the paper already written, at least had the results dropped in, rewrite the discussion, and within 60 days, have something ready to post on a preprint, and be ready

to submit to a journal.

That would be research done differently. I just think if this body wants to take some risks and move things in a different way, we have to start looking at this.

If we are really talking about dissemination, then we are talking about shortening the study period because we are trying to engage people so retention can go on in a much more efficient way, and then we are saying to investigators, you be ready on the last day to sprint, because we want to know the results ASAP, have the programs written, the papers outlined, everyone is lined up and ready to go for a 60 day sprint.

This is agile development. Anyone that knows about agile software development knows this is sort of like scrumming every day and do a sprint, and get this thing out, because we funded you and the expectation is this is important work.

If we are going to say we are actually funding work, we don't care, take a year and a half

after you are done with the study, and we look forward to it in that year and a half, and then we will go to folks and try to disseminate it, I think that sends a different message.

I know you are thinking why did I call on him.

[Laughter.]

DR. NORQUIST: That actually is a very important point.

DR. BARKSDALE: Actually, when we were going through writing this, we knew this would come up at some point. We felt we didn't want to reopen the peer review policy. I am going to suggest -- you raised some very important questions that quite honestly we have discussed internally a lot, and tried to put in place, like the limited competition D&I that we basically say, you don't submit your draft final report, you don't get any more money.

I am going to suggest let Joanna finish the slides, and then we can have at it with full discussion with everything on the table. We are running a little short on time.

DR. NORQUIST: Joanna, if you could go on a little quicker through the slides so we have time. We were reading them in advance. You don't have to read the slides, if you can kind of quickly finish.

MS. SIEGEL: Thank you. This piece that I'm coming to is about some poising, so we will take your larger points. I would like to talk about some of these selected findings and our activities that are focused on those.

To provide some context in terms of does this apply to all of our research, we have some findings that are already coming in, and we are in the process of initiating peer review of those findings. However, we anticipate many more results coming in at the end of this year, in 2017, and beyond.

In the near future, we are going to be looking at a much larger pool of results, and it is going to be important for us to identify and work systematically on dissemination and implementation, particularly for the highest impact findings. Of course, we won't know exactly what those are until

we have our results. We are ready to prepare for it.

This is a diagram that is intended to describe our strategy for selecting our priority findings and moving them towards dissemination and implementation. It includes identifying the findings, placing them within an evidence context, and setting the strategy for dissemination and implementation.

I am going to talk a little bit about each of these, but I do want to point out that although this is a linear sort of model, we are working on all of these pieces at once.

The first piece is really an opportunity for PCORI now to begin engaging in active surveillance to identify potentially high impact findings. We have large investments in certain areas of research like the targeted initiative topics and pragmatic clinical studies, and those are things we will automatically consider as potential priority topics for dissemination.

For the broad awards, we are developing a

process for flagging studies to help us identify early on the findings that we think have a strong potential for impact. The translation center, as I mentioned, will be reviewing the project summaries and the study findings, and we will be asking them to identify priority candidates.

The forms that the peer reviewers will be filling out and submitting has items that ask reviewers to comment on both the priority and the urgency of disseminating the findings that they are reviewing, and finally, we are working on a systematic process for capturing input from our program officers and program directors who have a comprehensive knowledge of these projects.

Another one I should also mention is that in some cases our engagement awards have involved activities that are going to be identifying projects that are of special relevance to certain stakeholder groups, and that is, of course, also something we would be following up on.

The next part of our strategy is to place the findings in the context of the body of the

evidence. That is to provide context and to understand the study's importance and how it fits with existing knowledge.

This piece requires coordination between PCORI's work in topic generation and our dissemination and implementation program because an understanding of the evidence context is important at both ends of the research spectrum.

In developing topics, review of the evidence helps us focus the research on the gaps where the new findings will have an important impact and as you know, PCORI's methodology standards prescribe gap analysis and systematic review should be used to support the need for a proposed study.

From the point of view of dissemination, a single finding is not often sufficient to motivate an important change in process. We will be disseminating findings as part of a body of research that comprises an evidence base. For some topics, we already have evidence summaries available. For others, we are going to be building a more thorough evidence context going forward. We just initiated

work to develop evidence maps like the one shown here for acupuncture on selected topics.

The last piece of the strategy is to choose an approach or more than one approach for dissemination and implementation of a selected finding or group of findings. This stage involves an active collaboration with AHRQ.

AHRQ has developed a framework for their dissemination and implementation initiative that includes a nomination process and involves separate assessments of strength of evidence and the feasibility of implementing specific research findings.

We and others have been working with AHRQ on piloting their nomination process and will be submitting nominations to them based on the criteria they are developing.

For PCORI findings that AHRQ selects as the focus of dissemination and implementation projects, the agency will be drawing on key informants who have a close familiarity with that particular area of research and practice, who will recommend what

they think are the best methods for disseminating and implementing research results.

We will be collaborating with AHRQ in this process, and as AHRQ is developing initiatives, we envision a lot of activities emerging that involve both collaboration on specific projects or for identifying areas where AHRQ and PCORI can pursue complimentary initiatives.

The future dissemination and implementation efforts we are envisioning are efforts that involve collaboration with or compliments initiatives that AHRQ is identifying through its process for findings from PCORI funded research.

We are also envisioning efforts that are tailored to specific findings, that is they are not generic strategies but are appropriate for disseminating specific findings to specific audiences, and we expect our initiatives will provide opportunities for awardees to have strength and experience in dissemination and implementation, and finally, we envision multi-pronged dissemination and implementation of important findings.

That is all I have to say except I did want to give a nod at least to our plans for evaluating dissemination and implementation activities. We do plan to use a number of short-term process type measures, including things like Web abstracts and continuing education certificates, things like that, but we also are exploring longer term impact measures that have effects on changes in practice and other types of outcome measures.

Thank you.

DR. NORQUIST: Let's go back to the discussion.

[Applause.]

DR. BARKSDALE: Before we continue, I just wanted to make sure that I introduce or reintroduce the members of EDIC who are all well versed in the content of this presentation, and that is Bob Jesse, who is co-chair. Gail Hunt. Sharon Levine. Larry Becker. Allen Douma. Sharon Arnold. I am missing Brian from the Methodology Committee, and I'm missing one person from the Methodology Committee, Mary Tinetti.

Now, back to Harlan's comment.

DR. NORQUIST: Bob Jesse?

DR. JESSE: I'll just add on to Harlan's point, and that is the level of urgency is probably not limited to this. As PCORI, we have some pretty tight time lines coming up, and everything we should do I think really needs to be pushed at that level.

In particular, working with our grantees, they just need to understand that across the board. We need to reflect that in our behavior, too, including having pretty tight time lines, I think, between RFPs and getting money out the door.

I think it is not limited just to this, but everything, setting a corporate tone for that level of urgency if we are really going to change the world.

DR. NORQUIST: Gail? Then Harlan, Leah, and Sharon.

MS. HUNT: Following on what I said this morning, I don't see a lot of attention being paid to implementation. I just heard implementation just mentioned in passing in a couple of these

PowerPoints and the presentation.

I don't think we have taken seriously the fact that we are expected to have results that will inform decision making at the patient and family and primary doc level.

Just coming out with dissemination is not really sufficient. I think we should be giving funding out for tools, development of tools that actually help patients and doc's to implement whatever the results are.

I'm very concerned this is an area that we have neglected, and we don't seem to be, even though we are rolling into like our last two years -- we don't seem to be focusing on that, and I think that is going to be a mistake when Congress says what has actually been accomplished at the patient level. I think we need to put more funding into it, and I think we need to have a plan for how we are going to do that and not just dissemination.

DR. NORQUIST: Jean, do you want to respond on that? Harlan, Leah, and Sharon.

MS. SLUTSKY: One of the things that we do

envision for those types of research findings that really are strong and fit within our body of research is to develop those types of tools and keep them updated to assist decision makers. Shared decision making tools, decision aids, other mechanisms to provide that information at the point of care.

One of the things that we have emphasized a lot is it is rare for one study to actually change practice. It is not unheard of, but it is generally research findings within the context of larger findings.

So, one of the goals is to create the infrastructure to make sure we can do that and support the shared decision making and decision aids and other activities that help people at the point of care.

I think we are saying the same thing. We are just going about it differently in that many of our smaller studies may need the boost of other studies to help them carry the water across the line.

MS. HUNT: I didn't see anything in the PowerPoints about tools and decision making instruments and that sort of thing, which I think if that is what you are actually planning to do, I think that is great, and I think we need to make it explicit. Thanks.

DR. NORQUIST: Harlan?

DR. KRUMHOLZ: I am yielding my place.

MS. HOLE-MARSHALL: I think this was great and I appreciated the materials. I think just building off what Gail said, I do think this is a very, very important area, and maybe what is not quite clear to me yet, and I'll put Sharon on the spot, and I apologize in advance although I don't expect you to respond, is I do think it is critical that we understand what the role of AHRQ is going to be so we can understand what other funding is necessary, and if it means amp'ing it up, I could be in support of that, but without knowing what the full set of activities are that are being planned, I have a hard time understanding where there might still be gaps.

I know this is a broken record at this point, but I really feel like when we have dissemination and implementation around PCORI, given there is legislative directed funds, AHRQ should be presenting on what it is doing with those funds. We have not had that to date.

DR. NORQUIST: Yes, I was going to put Sharon on the spot at the end. I was going to let you catch up. Do you want to respond now or do you want to wait and hear some other input?

DR. ARNOLD: I'm happy to respond now. We are doing a number of activities with our Trust Fund dollars. We have a large initiative that has just begun, developing clinical decision support tools and activities. We have other kind of tool development activities that we have consistently done to advance the dissemination and implementation of evidence.

We are now kind of gearing up for this nomination process, rather than us making the decisions, kind of scouring the literature about what the most important evidence is, we are looking

to important stakeholders from the field to nominate for us important evidence.

I might add that our scope is broader than just PCORI funded studies, so we are thinking about this as a range of evidence.

What we plan to do is assess the scientific rigor and strength of the evidence as well as kind of the environment for implementation, and by "environment," we mean are there tools, are there supports, is there a natural leader that can help implement this and direct our resources to where it will be most beneficial.

Unfortunately, given the nature of evidence and the environment, it's really hard to come up with an one-size-fits-all plan for dissemination, so we will really be targeting our approach to specific evidence and the environment.

I will say that we have a very large study that is ongoing now called Evidence Now, which is implementing health practices in small and medium sized physician practices. That is a good example of how we are targeting the support to the

environment and the evidence.

DR. NORQUIST: I guess the other question is the interface with PCORI. We're putting you on the spot here. The interface with PCORI, do you feel like there's an ongoing relationship so that it's very clear where the dividing line is or where we share or compliment, or whatever the term is at this point?

DR. ARNOLD: We have been working very, very closely with Jean and Joanna and their staff. I think that there will be a number of points of contact between us and them. One is the nomination process.

Obviously, PCORI is going to make a determination about what gets nominated to us, and then as we move along the process, we will collaborating very closely and consulting with PCORI staff about the different steps to take.

Certainly, when we make decisions about activities that we are planning or we think would be beneficial in support of implementation, we will be consulting with PCORI staff and making

determinations about what we fund, what PCORI funds, what we jointly fund.

We anticipate a very, very close working relationship. There is too much important work to be done for us to be both focused on the same activity simultaneously.

DR. NORQUIST: Thank you.

MS. HOLE-MARSHALL: Thank you. My question wasn't really that there isn't a lot of collaboration. We do hear about that, and not that good work isn't being done at ARHQ, it is just it's not surfacing through us.

We don't have an ability to help tell that story about here's things that are being funded through the PCORI Trust Fund that we can not overshadow ARHQ in terms of ARHQ's process, but say these are because of overall the PCORI Trust Fund, we don't have any visibility and aren't able to share in that, wow, here's a body of work that's being done based on this collaboration, however we choose to share that. That was my main point.

DR. ARNOLD: No, I appreciate that. I'll

certainly consult with Joe and Jean about how to provide that information.

DR. NORQUIST: Thank you, Sharon. Harlan K., Sharon, Freda, and Steve. Harlan?

DR. KRUMHOLZ: Thanks for the opportunity to elaborate just a little bit more. I guess a way for me to express this is like what would be an ideal state for me for this organization. The ideal state would be somebody gets a personal letter from Joe, appointing a grant, and saying we funded you because we believe what you're doing is important. We are very thoughtful about what we fund, and we think it's potentially of consequence. We wish you best of luck. We hope that you will finish this in a timely way. We're going to be tracking your enrollment, and it will be on our Dashboard.

We're going to be following, and if there are things we can do to help you, we'd like to know, because we want to be able to connect you with others or be able to ensure you're getting your study done in a timely way.

We also have hopes about what's going to happen from the moment it's finished. We hope that you will be positioned to sprint, to get this thing into the public domain as quickly as possible, that from the moment it's finished, you have already got your analytic programs written. You already have your paper outlined. You already have your team poised, and you are ready to sprint for the next 60 days to get this out as soon as possible.

You should know that we are also going to be tracking that. That is going to be one of our accountability issues. We have enabled the Board policy that has allowed as much as 13 --

[Webcast audio feed lost.]

[Recess.]

[Webcast audio returns mid-discussion.]

DR. WHITLOCK: -- treatment-resistant depression, new oral anticoagulants, treatment strategies for managing and reducing long-term opioid treatment for chronic pain and treatment of multiple sclerosis went through merit review late last week.

We are hoping to bring the slates back to you, and with approval, they will be awarded in summer of 2016.

An additional funding announcement, chronic low back pain, we are a little bit earlier in the process, but should hope to award that in winter of 2017, which means early 2017.

The three topics for today are management of sickle cell disease, what I would consider a follow on to the original opioid announcement, which was looking at reducing use, and those are chronic users, and this is to look at presenting unsafe opioid prescribing in primary care, and going a bit upstream.

The third is to look at community-based palliative care delivery for adult patients with advanced illnesses for both patients and caregivers.

Today is May 23, depending on your votes, we will take forward those that are approved to targeted PSA announcements on August 15, 2016. You will see the rest of the time line.

If folks are able to join us on the phone,

I just want to mention that I will be going through the slides relatively quickly because the Board has had access to these, but they will be on the Web site, so that as people learn of these upcoming funding opportunities, they can look at the slides, get an idea, more in-depth idea of what we will be looking for, and even begin preparing your applications soon.

DR. NORQUIST: I just want to clarify, the application deadline, the applications are in by December 19, but the merit review is not until March, the last of March? It takes three months?

DR. WHITLOCK: That is the time line.

DR. NORQUIST: I understand. It just seems like a long time between the applications in and the ability to have the merit review.

DR. WHITLOCK: We can talk about the time line off line, but these are standard time lines. That is the actual in person meeting, and there are many steps that take place prior to that. I am happy to show you the full detailed time line.

Let's go to management of sickle cell

disease. The goal of this funding announcement is to generate evidence that will support care transitions for young adults who are going from pediatric to adult health care in what is considered an emerging adult, which is somewhere around 15 to 25 years of age, in those with sickle cell disease.

As many of you know, sickle cell disease is a chronic, somewhat rare but serious genetic disorder, between 70,000 and 100,000 Americans, predominately African Americans, have sickle cell disease. The onset is during infancy, and there is a reduced life span in folks with this disease, and only relatively recently have folks been living long beyond childhood.

It turns out that those that are developing and aging into the young adult population are quite vulnerable to having worse health outcomes during this period of time, during this transition. This is the target population that we are focusing on in this targeted funding announcement.

Care transition is always an issue, but it is particularly an issue for youngsters who have

congenital heart disease or serious disease as children and then transition into adulthood.

It is somewhat different than thinking about going from hospital to home. It is really as children grow into adulthood, they experience the cumulative impact of the disease, and they have relatively high rates of comorbid conditions.

They also are experiencing a change from their usual source of care to a different source of care. In that transition, there can be difficulty getting access to specialists, such as hematologists, particularly if their source of insurance changes, and both adult care clinicians and these patients are not satisfied with the kind of care they are able to both give and receive.

By loss of usual source of care, often special care that is focused in pediatrics, it is documented that they have less preventive and screening visits and that the source of their care begins to shift, and they are more likely to actually go to the emergency department than other age groups.

The timing for this funding announcement is opportune in a number of ways. One is that we have the opportunity to build on work that is happening from other funders, including the National Heart, Lung, and Blood Institute. They will soon announce the results of a competitive funding announcement that will be funding research consortia around the country that could actually participate in this research.

Similarly, to our own PCORNet, we have some of our clinical disease research networks that are developing sickle cell disease cohorts.

Although this would be a good opportunity for applicants to work through existing research networks, and we would encourage it, it certainly will not be required. All will be able to apply.

I'm going to quickly cover evidence gaps. This is an expert panel report from 2014 from NHLBI. It shows that there are guidelines but they are based on weak evidence or consensus opinion, and particularly in the population that we have talked about, the emerging adults, they are the highest

rates of complications and of mortality compared to other age groups, but a real lack of evidence about how to improve care during this time period and health outcomes.

There is just very little evidence right now that is looking to try to fill these gaps for this vulnerable population.

We got together a workshop, and you will see we got together a multi-stakeholder workshop on March 7 of this year. For this particular section, 38 stakeholders of the variety seen here participated, and they submitted 59 questions prior.

These were consolidated into two major areas, the area of care transitions that we were talking about, and an area of pain management. Each group broke out and developed questions around each of these two major themes.

For the purpose of this funding announcement, we are focusing just on one question because that seemed to raise to the top, which is really about the issue of transition coordination models, different types of models for these emerging

adults as they transition from pediatric to adult care.

As I said, the population is what is considered emerging adults, generally defined as 16 to 25 years of age, although the transition can happen in a very focused time, 16 to 18 or may even be prolonged, depending on insurance coverage, up to age 26.

There may be interest in expanding the age group of those considering under transition if applicants are looking at issues related to insurance transitions as well as age related and practice related changes that are happening.

The interventions and comparators that are of interest are those that are incorporating all of the relevant partners, the patients, the caregivers, and the clinicians. There needs to be a robust patient engagement.

During the stakeholder engagement meeting, as the researchers and other community members talked about this, they realized because it is a rare disease and there isn't as much research, it is

going to be important that either something has been shown to be efficacious in sickle cell disease, it has evidence of efficacy in other diseases, such as diabetes, cystic fibrosis, congenital heart disease, where children also have to undergo a transition to adulthood, or it is something that is in common use.

There are examples here with acknowledgement that an usual care may be an appropriate comparator.

The outcomes are focused on health related quality of life, other patient important outcomes including social functioning and experiences of care, with secondary outcomes looking at hospitalizations and hospitalizations due particularly to pain crises.

The study design we anticipate is a cluster randomized control trial with sufficient sample size and clusters to power study. The focus would be on outpatient settings, a maximum of a five year study. The team felt a proposed research commitment of up to three studies and $25 million of total costs across all studies would be appropriate.

I will stop there and turn it over to Bob to lead a discussion.

DR. NORQUIST: Bob, do you want to give any feedback? This went through the SOC.

DR. ZWOLAK: This went through the SOC. I was the SOC champion for this. I felt it was an appropriately chosen and well discussed research topic. I would endorse this, and Evelyn and I will be happy to try to answer any questions.

DR. NORQUIST: Let's open this up for questions or comments at this point. Does anybody have any questions or comments? Allen, wait, Harlan Krumholz is up first, I'll come back to you.

DR. KRUMHOLZ: I just want to say I think it is particularly timely to come out with this. There has been a lot of discussion in the recent weeks about whether this has been a neglected area, actually putting it beside the moon shot, so I think it is actually really great that we happen to have been moving in parallel, and I think this will get some good attention with regard to the importance of the topic. I just wanted to commend the staff.

DR. WHITLOCK: Thank you.

DR. NORQUIST: I would agree. I see a fair number of these younger people because they obviously have a lot of mental health issues, and in public sector facilities and stuff, this is a huge population, and an issue, and has been for quite some time. I think some people would agree it has been a neglected population that for some reason has not come up on the forefront, so I would agree with that.

Allen and then Sharon Levine.

DR. DOUMA: With Bob's hearty endorsement, I would certainly endorse it as well. He knows a lot more than I do. I do have more of a generic question. How long a time frame from the last landscape review for doing evidence mapping, and our research, do we think it is too long, that we need to relook? Do you have a criteria for that?

DR. WHITLOCK: Let me see if I understood the question. Did you say --

DR. NORQUIST: Let me just be clear, Allen. It sounds like you are talking about the broader

process, not particularly the issue about sickle cell disease, right?

DR. DOUMA: Correct. You mentioned in 2015 somebody had done a review and found there is evidence gaps. I questioned how long a time frame between the last review and our decision making is reasonable.

DR. WHITLOCK: Well, depending on how complicated a field is, two years might be a time in which you might need to update. The sad fact is many of the researchers that work in this field were in the room for our stakeholder engagement panel, and there is a dearth of research.

We looked at Clinicaltrials.gov as well. There was nothing covering this area. I think in a more active field, you might be concerned about state of the evidence with a two year gap, but in this particular area, particularly given the fact there was so little there and we had researchers in the room, I think we are on very solid ground in terms of evidence gaps.

DR. NORQUIST: I think the answer is you

surveyed what evidence is there, it is just not a lot has been funded.

DR. WHITLOCK: Yes, not a lot.

DR. NORQUIST: It's not like we are off that much. Sharon?

DR. LEVINE: Evelyn, you referred to this, but there are many conditions now that used to terminate in childhood, where there is this awkward phase of hand off between the pediatricians who have taken care of these kids for 15 to 18 years and internists or family physicians who have never seen them.

The findings from this may be well applicable to pediatric congenital heart disease, cystic fibrosis, and other conditions where life spans are elongated, survivors of childhood cancer.

DR. WHITLOCK: Right. I think that was one of the encouraging things to the stakeholder panel, they said if we have to build on efficacious research, well, we don't have very much. The idea that you can think about the general condition of these congenital long-standing serious diseases in

childhood making a transition could help, as you say, across the board.

DR. NORQUIST: I agree with Sharon that it also has implications for management of chronic disorders, because we get into issues about pain and other kinds of issues like that that are critical. Mental health issues.

Any other comments or questions?

[No response.]

DR. NORQUIST: I need a motion to approve this development of the RFA.

M O T I O N

DR. McNEIL: So move.

DR. NORQUIST: Second by Kerry Barnett. All those in favor, please raise your hands.

[Show of hands.]

DR. NORQUIST: Anybody voting against?

[No response.]

DR. NORQUIST: Anybody abstaining in the room?

[No response.]

DR. NORQUIST: Allen, how are you voting?

DR. DOUMA: I agree.

DR. NORQUIST: Harlan Weisman, he dropped off the call. I don't think he's back on.

DR. WEISMAN: No, I'm on. I vote to approve.

DR. COLLINS: Francis Collins has joined again, and I am voting to approve as well.

DR. NORQUIST: Thank you, Francis. That is it. Evelyn, next topic.

DR. WHITLOCK: Thank you. The next topic, as I mentioned, is what I am going to be calling a sequential PPFA or targeted funding announcement because the genesis of it really came from recognizing that we could use more work in an area that we had already put a funding announcement out for.

The purpose of this proposed targeted funding announcement is to generate evidence that will prevent unsafe opioid prescribing while ensuring that adequate pain management is present for patients using one of two related intervention strategies.

The first would be looking at payer or health system strategies that make sure they are linking these two important activities together. The second would be looking at patient and provider communication interventions that would help look at benefits and harms of various treatments.

The background, as I mentioned, is the related funding announcement from October of 2015, looking at managing reducing long-term opioid use in chronic non-cancer pain patients. We are hoping to make up to four awards of $40 million in July of 2016. This, as you will see, funding announcement is complimentary to that initial one.

There are many evidence gaps in this area. There is wide variation amongst states in opioid prescribing rates, and there is lack of consensus as the CDC has pointed out. There is little evidence on how to prevent unsafe prescribing of opioids, and as much of the research to date is really focused on those patients that have already moved on to chronic opioid therapy.

We went through and even in recent

systematic reviews and other research, we could not find much evidence to look at, clinical outcomes. There are strategies that people are developing because as everyone knows, there has been a crisis in opioid overdoses and deaths and increasing levels of prescriptions, but few if any have been rigorously evaluated.

It is very important, people are given opioids and use opioids usually because they are trying to manage pain, and it is important that we find a way to link effective pain management and safe use of opioids together.

The question here is to look at two different modalities, both of them comparing effectiveness of different strategies either at the payer or health system level, or at the patient and provider communication level, to prevent unsafe prescribing while ensuring access to non-opioid methods for pain management.

The overall goal is to reduce pain, improve patient function and quality of life, and reduce patient harm.

For the first research question focused on payer and health system strategies, the population -- this will be the same for the other -- they are both focused on new users of opioids or patients who have used opioids for less than three months, and they can have either acute or chronic pain.

The context of use is outside end of life care nor those that are being treated for cancer, the type of patients we are looking for.

We are looking at interventions that are multi-focused, that look at preventing unsafe prescribing while also ensuring adequate or improved pain management. Interventions must be either evidence-based or in widespread use.

The primary outcomes are patient-centered, pain, quality of life, function, and also reduction in unsafe prescribing. Secondary are a range of patient-centered outcomes as well as impacts on providers, and emergency department utilization.

We are anticipating a cluster designed randomized control trial since these are system or payer level interventions. We are encouraging two

active comparators plus usual care. It would be possible also to do a large prospective observational study and it might be possible that mixed methods would be helpful since these are aimed towards complex settings potentially in their implementation.

The focus is on primary care since that is where many of these prescriptions are generated, but that is broadly defined. It includes emergency departments, primary care practices, dentist office, and urgent care centers.

We are anticipating a time frame of about three years with the sample sizes of 600 plus, and the commitment that we thought was appropriate given the range of different strategies that might be looked at as well as the different types of settings could be as many as three studies spending a total of $15 million.

The second research question focuses on also comparing different strategies that would improve communication around pain management and appropriate use of opioids, the same patient

population, new or relatively short-term users, for either acute or chronic pain.

The interventions must also address the two components, issues around preventing unsafe prescribing and also ensuring pain management is adequate or even improved. The interventions should be evidence-based or in widespread use, and may include combinations of various strategies.

Depending on what is chosen, two active comparators may make sense, but it may depend on what the applicants suggest.

You will see the primary outcomes and secondary outcomes, and you will see they are both patient level and provider level outcomes, and are the same as they were for the first research question. There is quite a bit of overlap in the outcomes that are being looked at through these two different strategies.

The study design would be a single individual randomized control trial or cluster randomized control trial, again focusing on primary care. Time frame of about three years, 1,700 or

greater, with multiple follow up data points, and we believe that for the same amount of money, $15 million in total costs, we probably could fund three to five studies, since these may be somewhat smaller.

I will stop there and see if Bob would like to make comments and lead a discussion.

DR. NORQUIST: Bob, do you want to make some comments first for the SOC?

DR. ZWOLAK: Very few. I just think this is one of the most timely and important issues we can address. It is a different population from those people who are already on significant doses of opioids, best to try to prevent the problem than deal with it once we have developed it.

I think these may be challenging studies to recruit for in the primary care setting, but very important.

DR. NORQUIST: Harlan, and then Barbara.

DR. KRUMHOLZ: I just have a technical question. Since these are continuous outcomes, patient reported outcomes, why does it end up

requiring so many patients? I just sort of imagine that you would have been able to do a variety of different trials with fewer patients given the continuous nature of the outcomes.

DR. WHITLOCK: I don't know that I have all the details on the sample size. I was just looking at that, because I anticipated there would be a question on that. Let me just look here.

We have not just continuous outcomes on patients but we also have the provider prescription rates. For question two, the sample size justification was a baseline rate of recurrent narcotic prescriptions at one year, and an one-third reduction.

The literature says about 12 percent with acute pain have a recurrent narcotic prescription at one year when presenting to the emergency department. You reduce that by a third, then that is how we came up with 1,700 total or 850 per arm.

The first one, let me see if I can find it. I also have -- if the phone was working --

DR. NORQUIST: Actually, the phone is

working now.

DR. KRUMHOLZ: You did actually do rates as a primary outcome in the second one.

DR. WHITLOCK: Right. We had to do both, so there would be less power for that.

DR. NORQUIST: Barbara?

DR. McNEIL: I actually have a similar question, Evelyn. This is such an important problem, if I link your data with the earlier presentation by Joanna and her colleagues about the time frame for dissemination and the fact that after a study was ended, there was 13 months for the final report, and then X months after that for a major dissemination activity.

We are talking four or five years potentially for the most important problem in the country today. I am just wondering isn't there any way we can compress the time line by getting a lot more patients through a lot more sites. I don't know how we would do this, but I think this is a critical study, but the time line just seems way off for me, for the nature of the problem. I think this

is going to be a why did it take so long kind of study.

Could we talk about that a little bit? I understand the power calculations given the number of sites, and I certainly relate to Harlan's comment about the continuous sets of outcomes. I really think we need to do something to cut down the time.

DR. NORQUIST: We can talk about that. Evelyn, there must have been some discussion about the time.

DR. WHITLOCK: I don't think so. I think this is a good comment, and I think certainly if we go back to the time line, if you decide to approve these today, we will be working on the targeted funding announcements, and certainly we can go back and consider whether it would make sense to try to expand the --

DR. NORQUIST: You are writing the PFA, we are not funding on X study now, so we could ask people to come up with ideas about how they might be able to do this quicker, I mean a shorter time line.

DR. WHITLOCK: Correct.

UNIDENTIFIED: This is Penny. I'm a program officer that worked on this particular announcement. It is actually three years for both of the studies, so it is not four to five, and we had encouraged the compressed time frame.

DR. NORQUIST: No, she is talking about also when the results come out. Go ahead, Barbara.

DR. McNEIL: No, I understood the three years, but then I was very concerned with the earlier presentation about the final report and the results. Isn't there a way of just telling people we want results in a year and a half and saying get the population to do it? That is your job.

DR. NORQUIST: Yes, I think the other issue is whether you expect to get an endpoint on some of your outcomes within a year or two. That might be the other limitation on the time here, I don't know.

UNIDENTIFIED: Hi, this is Brittany --

DR. NORQUIST: Wait, I'm sorry. We need a little bit of order here. Evelyn is getting ready to say something, and then I will let you come in.

DR. WHITLOCK: What I was going to say was

I think we can look at the critical nature of the information that would be reduced here, see if there is any way we can give priority to folks that could produce the information more quickly considering both the recruitment rates, as well as the time frame to the outcomes.

As was talked about earlier, perhaps it is possible for us to write in, talking about whether we can say to people that people have to guarantee they are going to get their reports back to us in a short period of time for this particular topic.

DR. NORQUIST: That was the discussion we just had about trying to push the time period and shorten that. I think not only with this one, we are going to be pushing it for others, too.

DR. McNEIL: Getting the study finished, but the dissemination activity done, really compress the whole --

DR. NORQUIST: That is what we were just talking about, both pieces, both parts of what make up the whole time line here. Someone on the phone wanted to say something, so if you want to do that,

and we have some people here in the room that are going to make comments.

UNIDENTIFIED: Thank you. Evelyn covered the comment I was going to add.

DR. NORQUIST: Okay, thanks. Sharon and then Leah.

DR. LEVINE: One of the thing that is important about this is there is already a lot of natural uncontrolled experiments going on, everything from just say no to real efforts to try and address the problem.

One of the things I'm struggling with is your definition of "primary care" including emergency departments and dentists. I don't think emergency department physicians consider themselves primary care physicians, and the nature of the problem is different in emergency departments, dental offices, and what we traditionally consider primary care adult family medicine offices.

The problem with dental practices and with post-op patients, if you will, is the default size of the prescription, defaulting to 100 Vicodin as

opposed to 6.

There are a lot of subsets of this, and I think if the TPFA was written to identify the optimal approach to addressing different aspects of the problem, which are rolling up into a massive over prescribing of opioids, we might be able to see some things accomplished very quickly.

DR. WHITLOCK: I think what you will notice in these presentations is that we are a little bit less prescriptive perhaps than we have been in previous targeted funding announcements to leave room because of exactly what you are saying, that the optimal strategy for the ED could be well different than the optimal strategy for the family or adult medicine person, but I think your point is we want people to justify why what they are proposing is an optimal strategy for that environment and is comparing optimal strategies for that environment. That is a really good point.

DR. LEVINE: The other thing is we have already seen, I think the number of prescriptions of opioids in 2014, so there has already been about a

13 percent decline, not in the number of pills dispensed, but in the number of prescriptions.

DR. WHITLOCK: Yes. There is definitely still room for improvement.

DR. NORQUIST: Leah?

MS. HOLE-MARSHALL: Thank you. This is an important topic, particularly to me, and I appreciate seeing it come to fruition and appreciate all the efforts of you and the staff to get it here.

I just wanted to second some of the comments that I heard. I think that we could without over prescribing the study in the TPFA point out some of the issues that we have heard today acknowledging urgency versus the tradeoff potentially of certain outcomes that we are interested in, whether or not interim reporting of certain outcomes would be appropriate, and then seeing the principal investigators respond to things like that.

It may make our merit review more difficult if we are trying to -- they addressed this piece of it, and may address that piece of it, but as long as

we were clear.

Then some carrots, maybe this is a potential for us to experiment a little with carrots related to if your proposal is one where you recognize this urgency and also are agreeing to shorter time frames on other things that don't impact outcomes, like reporting, you will get a five percent bonus, however you would score it, but letting them know that we are not going to change the requirements for everybody, but there might be carrots for certain things, where it is appropriate.

DR. NORQUIST: I don't see any others. I think one thing I would say is that NIDA is very interested in us doing this, National Institute on Drug Abuse. It is not an area they have really been into. I think we should say that also as one of our partners in some of the work that we have done on substance use.

DR. COLLINS: I wanted to also endorse what you just said, Gray, and also to say that I think particularly the way in which these are designed, and I think particularly the first one, the

opportunity to try to recreate the settings that traditionally were more available than they are now, mainly pain clinics, where you explored a variety of ways of pain relief outside of opioids, which has almost disappeared from the landscape in large part because they are not reimbursed.

We have to figure out a way to reintroduce some of those non-addictive alternatives. I assume that is a big part of what you are trying to achieve in the first of these two.

DR. WHITLOCK: That's correct.

DR. NORQUIST: I need a motion to approve. Steve?

M O T I O N

MR. LIPSTEIN: So move.

DR. JESSE: Second.

DR. NORQUIST: All those in favor, raise your hand in the room.

[Show of hands.]

DR. NORQUIST: Anyone opposed?

[No response.]

DR. NORQUIST: Anyone abstaining?

[No response.]

DR. NORQUIST: Okay. Francis, you are voting how?

DR. COLLINS: Approve.

DR. NORQUIST: Harlan Weisman?

DR. WEISMAN: Approve.

DR. NORQUIST: Allen Douma?

DR. DOUMA: Approve.

DR. NORQUIST: Okay. Bob Zwolak?

DR. ZWOLAK: For clarity sake, I wonder if we could discuss for a minute the concept of writing in this urgency issue. Is that generally supported? I am worried about Leah's question of potentially even a financial incentive for urgency. I don't think that would work very well, but certainly writing the urgency concept into the PFA --

DR. NORQUIST: I think that is kind of a key issue for all of them. I think this is an urgent issue. I think all of the things that we are doing should be considered -- it is the most reasonable thing to do.

I think this one in particular certainly

has a big -- there is an IOM Panel now that is being formed by the FDA to look at opioid issues. I think within reason. Barbara?

DR. McNEIL: Is there any way of putting into the announcement something -- this is not the right wording, but preference will be given or consideration will be given to the length of time for completion of the study?

DR. NORQUIST: Rating it higher?

DR. McNEIL: Yes.

DR. NORQUIST: I guess we could put that in that we are very interested in those that can be done in a much more expeditious manner or something, and we do expect the results to be available readily or something. You will have to come back with whatever the wording is on that, we are just making it up now. I think you are getting the gist of what we are saying.

Last but not least -- I'm sorry. Christine had her card up. Is that Allen?

DR. DOUMA: Yes, it is.

DR. NORQUIST: Christine?

DR. GOERTZ: I agree about trying to expedite things, but we have to remember there is a tradeoff between expediting results and length of follow up. We want to make sure we are not encouraging people to come in with really short lengths of follow up that really impacts the usefulness of the study.

Just one thing, I think it said these grants would be funded in July of 2016 on the slide. I just wondered if you could clarify the time line.

DR. WHITLOCK: It should be -- hold on. I think it is May of 2017.

DR. GOERTZ: Great, thank you.

DR. WHITLOCK: The PFAs would be released August 2016 and it goes from there.

DR. NORQUIST: All right. Allen?

DR. DOUMA: My question was directed to that, how long before we actually start, and that May start date, is that when the project actually begins or when funding starts?

DR. WHITLOCK: May 2017, I'll show you the time line at the end, but what you vote on today, we

will get the targeted announcements out by August, and then we would plan to have you vote, it is on the schedule for you to vote in May, so then we have to set up the contracts. That is how it works.

DR. NORQUIST: They would not actually be starting and funded probably until the summer of 2017.

DR. WHITLOCK: Yes. I don't know all the time lines.

DR. NORQUIST: I think that is one of those things I said earlier, if there is a way to even compress somewhat our whole process of getting to that, I know that's not easy, but that might be another piece on the front end we could compress.

DR. WHITLOCK: The one thing I do know is you can prioritize some things, you just can't prioritize everything. I take the point that opioids, if there is anything we can do a fast track on, this is definitely one that we should do our best to do. I take that point.

DR. NORQUIST: Okay, maybe that is one we can speed up. We will see.

DR. WHITLOCK: We will do our best.

DR. NORQUIST: I know you will. Where are we? Palliative care.

DR. WHITLOCK: Now we are on palliative care, and thank you for all of the good ideas and input. This targeted funding announcement is looking at community-based palliative care delivery for adult patients with advanced illnesses and looking at the impact on those patients and their caregivers.

There are two separate goals for this. The first is to support advanced care planning over time, and make sure that it is consistent with what are patients' goals and preferences. Then to support the delivery of community-based coordinated palliative care that implements those care plans.

As many of you are probably aware, palliative care is under delivered but very important. Palliative care is more than hospice. Hospice is just a setting for delivering palliative care.

In those that have advanced serious

illness, there is a significant burden on them and on their caregivers in terms of symptoms and quality of life, and systematic reviews show getting palliative care can make a real difference for patients and for caregivers.

There are a number of components of palliative care which include systematic assessment and management of patient symptoms, psychosocial support for patients and caregivers, advanced care planning, and coordination among different clinicians, to facilitate goal concordant care, and you will hear that "goal concordant care" again and again because it is in some ways maybe the gold standard of outcomes in this area, that people get the care that they really wanted to get at the point in their illness trajectory that they receive care.

There are many different perspectives that have gone into developing this funding announcement. This funding announcement tries to address the fact that palliative care is typically limited to end of life hospice or in-patient hospitals, and not where patients live in the community, that we don't have a

huge workforce of palliative care specialists, and community clinicians are under prepared to work in this important area.

Decision makers, systems and payers need to know the comparative information on the most effective and efficient ways to deliver palliative care in the community, and that even at the level of the World Health Organization, people are being encouraged to emphasize delivery of palliative care services in primary care communities and home-based care.

This is also, I think, a very timely opportunity for PCORI in terms of funding. On January 1, 2016, Medicare approved reimbursement for advanced care planning discussions, and they can happen repeatedly as is recommended.

Also, payment reform through the Affordable Care Act incentivizes delivery of high quality coordinated care, and similarly to several of the other PFAs I talked to you about, there are research infrastructure opportunities that are federally funded that make research in this area very timely,

and other researchers recognize that PCORI in particular is well positioned to do this kind of work.

There are evidence gaps that are limiting the implementation of advanced care planning at this point. Most studies of advanced care planning look at one time interactions, look at relatively short-term outcomes, and don't look at what I told you was probably the gold standard, which is goal concordant care. Most of them don't look at an integrated approach, looking at both patient focused interventions and clinician focused interventions.

So, there are gaps suggested by systematic reviews in terms of how best to understand what are the effective elements of advanced care planning and how best to implement it into standard care.

The first research question focuses on advanced care planning, looking at different communication and combination approaches that focus on patients, caregivers, and clinicians, that look at facilitating advanced care planning discussions.

There is a focus because these prior

research and the application of these services have been generally limited. There is a focus here on getting geographically, racially and ethnically diverse patients that are living at home, and to try to move beyond a focus on just one area to looking at any advanced illness, and those who experience a high symptom burden.

Examples that we would encourage are advanced heart failure, advanced COPD, advanced kidney disease, advanced neurodegenerative diseases, cancers would also be considered, but we would like it if folks would be a little broader than some of the prior research has been so that it is more generalizable.

The idea is to focus on efficacious or widely used programs and interventions that facilitate advanced care planning conversations and documentation of these goals in the patient record, and that will look at these over time.

If you look at this schematic, it is really just to emphasize that the orange blocks focus on the interventions that would be looked at in this

PFA, patient and caregiver directed preparedness, and clinician directed training and preparedness, and on the left is patients with advanced disease going through a series of discussions, updated discussions, and then receiving goal concordant care on to the setting of death.

At the bottom, you see proximal, intermediate, and distal outcomes. These announcements will emphasize the measurement of distal outcomes, which have rarely been measured in the research to date. Goal concordant care, setting of death, and the impact on bereavement. The idea is to really look at the ultimate health impact.

The timing would be up to five years in order to get these distal outcomes. We would want to have multi-site community-based settings, such as hospital-based clinics, solo or group physician practices, and patient homes. We would not address institutionalized settings such as hospice and nursing homes in this announcement.

We would like to see a randomized control trial or cluster randomized control trial, mixed

methods, because of the inherent diversity of patients as well as settings that would be studied. Our sample size desire would be 750 plus patient and caregiver dyads with multiple follow up data collection points.

We believe with a commitment of $18 million total dollars that we could fund three to five studies, and that would give us a nice start on information that could inform the delivery of these services to patient advantage.

The second -- I will be almost finished, and thanks for your patience in listening -- the second area that will be focused on in this PFA is looking at models of care that deliver community-based palliative care.

There are efficacious models but it's not clear how people should decide between them, and the organization and the delivery of palliative care in community settings. There have not been multi-site studies.

Generally, as we referred to in an earlier population, there has generally been a very limited

focus on selected illnesses and narrow groups of individuals, and it would be helpful to standardize outcomes and provide some head to head comparisons.

This particular question does focus on the comparative effectiveness of different established models of palliative care in the community, and the impact on patients and their caregivers. Same population as the earlier question.

The interventions and comparators differ in that they are looking at different models of established care that differ in their level of integration between primary and subspecialty clinicians, that differ perhaps in the site of where they are delivered or in the method of delivery. You will see that remote and tele-medicine are on here for the possibility of rural delivery.

The outcomes are patient and caregiver quality of life as the primary outcome, along with symptom burden, distress, and receipt of goal concordant care, as we have talked about, and then secondary experiences around satisfaction, utilization, and out-of-pocket costs and expenses.

These are also up to five years, similar kind of setting as the first question, and we believe in having a cluster or randomized control trial, having a sample size of around 1,000 plus patients and their caregivers, so a total of around 2,000 would make the most sense. I can give you some rationale for that, if you would like.

We believe that the commitment of $30 million total dollars will fund up to three studies, and that would provide a lot of information for the field in this important area.

I will stop there. I went through the time line earlier, this is just a reminder of the time line for any of those you approve today. I will turn it over to Bob.

DR. ZWOLAK: Thanks, nice job. The SOC looked at this in detail and endorses the plan provided by Evelyn. I think that any effort we can make to shine the light on advanced care planning in the community before our loved ones show up in the acute care hospitals for their last admission is something we really need to do and help figure out

how to make it work right.

This is another important topic that I think should be a targeted PFA.

DR. NORQUIST: I saw Larry's card up first, and then Sharon Levine.

MR. BECKER: I just wanted to test my understanding. I think Bob's comment clarified for me, but just let me test this, and that is some parts of these studies will include call it "education" for patients and their families before they ever get to being sort of in the bed.

DR. WHITLOCK: Yes, I think advanced care planning discussions can happen at any point. One of the good things is because Medicare is now reimbursing for this. We hope that more clinicians will be having these discussions with their patients and their families, and then updating those discussions over time.

I think there is an enormous opportunity for us to do research as well as to shine the light on how important the practice is.

DR. LEVINE: I would hope that one of the

research proposals involves looking at what is happening in La Crosse, Wisconsin with the Gundersen Health System, which has a phenomenal program called "Respecting Choices," which is a community-wide effort, and advanced care planning begins when you are 55 whether or not you have an illness yet at that point.

What they have been able to demonstrate is by incorporating it into routine care after the age of 55, and it begins with what they call "first steps," which is identifying the "what if," who would you want to make decisions for you, and then revisiting it at every routine appointment.

When someone develops a chronic or life threatening illness, the path has been so well paved that those conversations don't fall to the poor oncologist to say oh, by the way, you know, there are some things we need to talk about.

It is a fabulous model, and it has been seated in places around the country. I am hoping somebody includes it as a comparator.

DR. WHITLOCK: I'm wondering if just based on your comments, we have RCT or cluster RCT, if maybe we should allow in a large observational study.

DR. NORQUIST: Allen, then Harlan Weisman, and then Alicia. Allen?

DR. DOUMA: I just think we ought to reinforce it is incredibly important, and my concern though is if you look at the community-based models that were listed here in our handout at least, all three of them, bottom line, look really a lot alike, assuming after somebody gets a referral, they go and utilize the services.

My concern is we are going to show these all look pretty good, but we're not going to prove anything, because we don't have a comparative with something that doesn't work.

DR. WHITLOCK: Thanks, Allen. Are you suggesting then that there should be an usual care comparator at least in some of these? Is that what you're saying?

DR. DOUMA: Yes, an observational study,

but RCTs, as we all know, are always more profound. Yes, I think we need to have something that is not great in order to show a difference. The same issue with regard to Hepatitis C, we can't assign people to something that is not great.

DR. NORQUIST: Harlan Weisman, your turn.

DR. WEISMAN: I just wanted to follow up on both Larry's question and Sharon's comment. I am really confused between question one clinical trials, and question two clinical trials, in terms of the patient population because they are identical, as far as I can tell when I read them both.

It's not clear to me which patients are going to which trial and which questions are more relevant for which populations, or are we saying it's the same population, two different sets of questions, how does advanced care planning and palliative care delivered, how are they interacting with each other in terms of the knowledge base that we are creating.

I was just wondering whether synthesizing

the two of them together makes sense, particularly given Sharon's suggestion of the kinds of patients that might be included are not in the definition of the patient population.

DR. WHITLOCK: Thanks for that. I think if we were -- this is just my opinion. If we were to deliver palliative care and advanced care planning appropriately, then we would be engaging with people more in advance of some of the illnesses.

It may be that if we take the population and rather than requiring they already have an advanced illness with a high symptom burden, if we also allow it to be just advanced stage, and we will let them define that because I don't want to define that. That was a joke.

Anyway, if we do that, it would make some distinction because there is a distinction between the advanced care planning discussions and the documentation, and then the actual delivery of services that help people to cope and feel better.

These two do compliment each other, but your point is well taken, and Sharon's point is well

taken, that maybe we need to recognize there often could be and should be upstream discussions around advanced care planning before people are quite at the point of needing a lot of services.

DR. WEISMAN: Since you are looking at long-term, doesn't the way the palliative care gets delivered impact the effectiveness of the advanced care planning? In other words, if you get the advanced care planning right, but you have chosen a wrong model, in other words, they are interacting with each other in a way that seems to me needs to be synthesized.

DR. WHITLOCK: We will take that under advisement, thank you.

DR. NORQUIST: Alicia?

DR. FERNANDEZ: Just two quick comments. I am familiar with these from the SOC, and I am very enthusiastic and supportive. One issue is I was hoping we could have something in there about sustainable and scalable interventions, and you don't need to respond to that now, but I know we brought it up before, and I am wondering whether we

can put that in.

There have been quite a number of very successful small scale advanced directive interventions, and I think where we can make a difference is in what actually works on a larger level.

I have another comment. The other comment is simply a logistical one of necessity, our time table between the time the PFA goes out and the LOI is due is like a month, a month in August or something.

I am wondering if there is a way we can work with -- this is not so much for you, but a way we can work with our specialty society colleagues once this PFA is approved, to get it out there, to make people well aware of this before the actual release.

I can't remember whether our LOI process is obligatory or not. It is, right? Otherwise, it will absolutely limit the number of people, and it just is not going to work. Not many people can write a grant or a good LOI in three weeks in

August.

DR. WHITLOCK: Thank you for both of those. We already have planned, as I mentioned, and probably I didn't say it clearly, we retain some details on these slides because we are going to be putting them up on the Web site as we always do, but pointing to them in a pre-announcement before the PFAs go out.

We actually are going to be putting out a pre-announcement. We're going to be targeting groups as appropriate, but we agree, we need to give people more time, and that's one way we are going to try to do it.

DR. FERNANDEZ: By "targeting groups," you mean working with the specialty societies?

DR. WHITLOCK: Specialty societies. I haven't got a complete strategy worked out, but it might be existing researchers in the field, things like that, where we know we can go to places where they will distribute these and make people aware, because we are trying to get ahead, as you suggested.

DR. NORQUIST: That is a good point, because the summer is going to be dead, in August, people are not going to be around and then come back suddenly. The sooner out, the better; yes.

DR. FERNANDEZ: What do you think about language on scale?

DR. WHITLOCK: It's fine, just know everything that is in the PFA can't be in these slides. I did well to keep all of this against editors.

DR. NORQUIST: Other comments?

[No response.]

DR. NORQUIST: I need a motion to approve.

M O T I O N

DR. BARNETT: So move.

DR. NORQUIST: Second?

DR. FERNANDEZ: Second.

DR. NORQUIST: All those in favor, raise your hand.

[Show of hands.]

DR. NORQUIST: Anyone opposed, raise your hand.

[No response.]

DR. NORQUIST: Anybody abstaining?

[No response.]

DR. NORQUIST: On the phone, Allen?

DR. DOUMA: Approve.

DR. NORQUIST: Harlan Weisman?

DR. WEISMAN: Approve.

DR. NORQUIST: Francis?

DR. COLLINS: Approve.

DR. NORQUIST: Okay, that's it. Thank you.

DR. WHITLOCK: On behalf of the science staff, I want to say thank you. We are all really excited about these. We are going to work our tails off to get these out and get good applications. Thank you.

DR. NORQUIST: Thank you, Evelyn, and all of the staff, and Bob, too, to the SOC and your folks, thanks.

DR. ZWOLAK: Thank you.

DR. NORQUIST: You don't go anywhere, Evelyn. You have the next one as well, right, with Christine.

DR. WHITLOCK: I have three studies that need to be voted on, with Christine.

DR. NORQUIST: These are additional awards from Cycle 1, one from the large pragmatic and Cycle 2 for the broad's, right?

DR. WHITLOCK: Yes. There are three studies, we are 15 minutes behind. I was supposed to have --

DR. NORQUIST: Wait, I just need to say that in this particular discussion, we have some people who are recused for conflicts of interest, so that is Debra Barksdale, Steve Lipstein, Alicia Fernandez, Andy Bindman, and Robert Zwolak. Okay, now you can go.

DR. WHITLOCK: David Hickam, are you on the phone?

DR. HICKAM: Yes, I'm on the phone.

DR. WHITLOCK: Dave, we are behind. We were supposed to be finished by 4:45. Dave is going to present the first study because I am recused from the study.

DR. NORQUIST: You're recused? That is not

on there.

DR. WHITLOCK: Cycle 1 pragmatic studies funding slate, comparative effectiveness of breast cancer screening and diagnostic evaluation by extent of breast density. Dave, can you take us through this real quickly?

I am on the additional pragmatic study, the name is in addition to the 2015 Cycle 1, and I'm on slide 130 with the research question. Do you mind taking us through this, please?

DR. HICKAM: Yes, thank you. This is David Hickam. I am a science program director at PCORI. I am going to briefly summarize for you an additional study that is being proposed to add to the previously approved slate for pragmatic clinical studies.

This is a proposed large scale prospective study with an observational design addressing the question of personalizing breast cancer screening on the basis of women's breast densities.

There is also a second aim of this study, which is a smaller aim looking at the contribution

of MRI imaging to the preoperative evaluation of women who screen positive for breast cancer after routine screening procedures.

The population of this study would be women between the ages of 18 and 64, including all stages of breast density from essential minimal density to the most dense breasts.

As I said before, this is a prospective observational study, it builds upon an existing infrastructure for doing prospective monitoring of women who receive breast cancer screening in routine clinical settings.

It is essentially in the first aim looking at the comparison of digital mammography alone to digital mammography with various supplemental screening modalities, the most widely used of those now is called "tomosynthesis."

Also, in further negotiations with these applicants, a question came up about variation in the reading of tomosynthesis exams based upon the experience of community radiologists, so that was added as a third aim, essentially as a substudy of

this project that had a minimal effect on the study's budget.

This study looks at fairly standard outcomes that can be measured over a reasonable period of time, including the rates of screen detected early stage cancers, the rates of later stage cancers, various types of patient reported outcomes having to do with women's experience with the screening process, and then some projected long-term clinical outcomes based upon basically state-of-the-art modeling approaches.

The second aim, looking at supplemental imaging for women who are undergoing further evaluation after screening positive, essentially looking at the success of treatment in those women.

The study's budget for this comes in at around $7 million. I think this is a typo in the slide. It says $8 million. It is close to $7 million for total budget.

It has really good engagement, and basically has an important potential impact because as many of you know, several states in the United

States are now requiring that women be informed about their extent of breast density with a breast density having been recognized as a risk factor for developing breast cancer, so this study will provide better evidence to guide clinicians in advising women about their screening options.

This would add one project to the previously approved slate of five projects in that round of large pragmatic studies, bringing the total expenditure up to somewhere in the neighborhood of $67 million.

We are basically calling for discussion and a vote by the Board of Governors.

DR. NORQUIST: We are open now for discussion. Rick Kuntz?

DR. KUNTZ: Thanks for explaining this, Dave. It looks really good. Can you very quickly tell me why you didn't want to do a randomization in this one? There are a lot of variables here. If not, just what kind of baseline controls you are going to ask for?

DR. HICKAM: Basically, in order to be able

to sort of look at a broad range of women by density of the breast, sample size requirements are quite large. This study will actually have an estimated sample size of higher than two million women based upon the multiple United States sites at which it will take place.

As you can tell, for doing a randomized control trial with sample sizes in that range, it is just not realistic.

DR. WHITLOCK: Just one clarification. It is actually one million women having about 2.5 million exam's, to be clear.

DR. HICKAM: I'm sorry, thank you for that clarification. Yes, you are right. I was counting exam's rather than women, sorry about that. Still, sample size is quite large, and a randomized control trial would require probably upwards of 10 years to be able to enroll that many women.

DR. KUNTZ: That is a good response. I just wondered if you could also just synthesize the rigor of confounding controls because you will get the wrong answer if you don't control confounding.

DR. HICKAM: This uses really state-of-the-art to control for confounding using both propensity score and instrumental variable techniques. We felt this really passed mustard in terms of using the appropriate adjustment techniques for controlling for confounding.

DR. DOUMA: Gray?

DR. NORQUIST: Wait a minute, Allen. Barbara was up next and then you.

DR. McNEIL: I have talked about this a lot at the SOC and with David and various people. I have to say I am still not enthusiastic about it, and I apologize for my continued lack of enthusiasm.

The first part of it relates to something that Rick just said, I think it is going to be very hard no matter how much you control -- excuse me one second. Maybe this is a sign that I shouldn't be speaking.

DR. NORQUIST: Barbara, we will let you drink some water and I'll let Allen make a comment, and then we will come back to you. Allen, go ahead. Barbara is taking a little break here.

DR. DOUMA: A lot of comments but a question. What is the time frame for completion of the study?

DR. HICKAM: The study would have a five year time frame.

DR. DOUMA: We are talking about 6 to 7 years before we get information out?

DR. HICKAM: I think it is a discussion that occurred a little earlier in this meeting, look to see the extent to which they would have interim results available and a shorter time frame, and how we could expedite sort of the final data analysis stage of the project.

DR. DOUMA: Are you saying that is the plan or that is just something we could consider?

DR. HICKAM: That would be the plan.

DR. NORQUIST: Barbara?

DR. McNEIL: Sorry. I think it is going to be very hard to control. I think Rick was right. Most people are getting tomo's, it is just the norm in most places. I think we have to account for that. The second part is people don't care about

learning curves. They care about the end result. I think I said that in an earlier meeting.

I would be very interested in knowing the accuracy of various kinds of radiologists as a function of location and number of exam's read at a particular point in time. As of yet, you haven't got there, and I think most people feel that way.

I would hate to be spending a lot of money to be actually getting a curve, when in fact the only thing that counts is the last point.

Going back to the first one, I think this whole issue of whether any mammographer is going to believe a result no matter how many propensity scores or instrumental variables we do, that hasn't been based on a full study of everybody getting everything is remarkably low.

By five years from now, I guarantee there is not going to be a woman in the country with dense breasts who is not going to have a tomographic study, and maybe there is not going to be a woman anywhere who is not going to get a tomographic study.

UNIDENTIFIED: [Inaudible.]

DR. McNEIL: Yes, but I don't do mammography.

DR. WHITLOCK: This study has been really carefully and extensively discussed at the SC level and we have had -- thanks to Barbara's concerns, I think there has been a lot of staff work in looking at how to make sure the study was scientifically sound and trying to address her concerns to the extent possible.

In the end, the SC did vote to recommend to the Board that this study be funded.

DR. NORQUIST: Harlan?

DR. KRUMHOLZ: I just want to clarify, and I have such respect for Barbara, I do think the Board in cases like these needs to be reflecting on process so that unless there is some major fatal flaw that wasn't appreciated and discussed in the prior area, that it is hard for us to be in the position, I think, to overturn the decision that went forward.

We have used this platform to be able to

express ourselves, which I think is fair and appreciated, actually, to hear what were some of the points of tension and decision, but I do want to say -- Steve Lipstein has brought this up many times, and I agree with him -- without that fatal flaw and if the process is to proceed, we need a strong process and respect that process. I think that has to occur throughout the organization.

I am both appreciating and trying to honor what Barbara is sharing but also saying as a board, I think we need to -- if we start violating the process, then the whole thing starts to unravel, and it undoes a lot of hours of work by members on all sides, so I want to endorse the decision and endorse the process.

DR. NORQUIST: Also, this did go through peer review, correct?

DR. WHITLOCK: Yes.

DR. KRUMHOLZ: Part of the process is review, then Selection Committee staff, that is what I mean, that whole arc of review. At this point, I think we should be focusing on whether the process

was followed well and respected.

DR. NORQUIST: Or is it within the portfolio balance or whatever, so the fiduciary issue. Sharon?

DR. LEVINE: Just a clarifying question and maybe Barbara is the best person to answer. How much congruence is there in interpreting degree of breast density among mammographers? Radiology.

DR. McNEIL: I'm not sure I know. Yes, I know a lot of congruence, the degree of, I'm not so sure. I think there is more variability there.

DR. WHITLOCK: That actually was data that we reviewed for the U.S. Preventive Service Task Force. It was 12, depending on which category changes, at least 12 percent mis-categorization or between sequential mammograms, so there is some degree of variability in the field on digital mammography.

Were you asking about tomosynthesis or digital mammography?

DR. McNEIL: Digital mammography.

DR. WHITLOCK: Yes. I just want to comment

-- are you finished, Sharon? I didn't mean to cut you off. In terms of the learning curve versus accuracy, we did ask for the ability to do that, and it can be done, but it is a fair additional cost, and we were trying to minimize cost. If we want to revisit that and we are willing to put additional money into it, it can be done.

DR. NORQUIST: Okay. I don't see any other comments. Anybody on the phone?

[No response.]

DR. NORQUIST: I need a motion to approve the funding of this particular announcement.

M O T I O N

DR. LEVINE: So move.

DR. NORQUIST: Second?

DR. GOERTZ: Second.

DR. NORQUIST: Any further discussion?

[No response.]

DR. NORQUIST: We are ready to call, and I will just remind you that Debra, Steve, Alicia, Andy, and Bob Zwolak cannot vote. All those in favor, raise your hand.

[Show of hands.]

DR. NORQUIST: Anyone opposed, raise your hand.

[No response.]

DR. NORQUIST: Anybody abstaining?

[No response.]

DR. NORQUIST: On the phone, Allen?

DR. DOUMA: Approve.

DR. NORQUIST: Harlan Weisman?

DR. WEISMAN: Approve.

DR. NORQUIST: Francis?

DR. COLLINS: Approve.

DR. NORQUIST: Now we have one from the broad, no one is recused, right? Mary? No one is recused on this one.

MS. HENNESSEY: Unless someone volunteers.

DR. NORQUIST: Unless someone volunteers, okay. I guess we will see in a minute.

DR. WHITLOCK: We will see if we can get through this pretty quickly. You may recall from the last time we spoke that you had approved several proposals for funding, and you can see that we are

suggesting adding one to each of the programs, Assessment of prevention, diagnosis, and treatment, and the improving healthcare systems.

The overall impact will be going from an overall funding level of about 16 percent to about 28 percent, if you decide to approve these.

In the first case, the additional recommended project is one that is looking at high intense periodic versus every week physical therapy in children with cerebral palsy. It would add -- you can see these other projects that were already addressed and approved.

The second would look at patient-centered Hepatitis C care via tele-medicine for individuals on opiate substitution therapy using a stepped wedge cluster randomized control design.

Each of these were part of the broad slate. They went through additional review and scrutiny by the Selection Committee. The Selection Committee was satisfied that both of them made sense within the overall portfolio, and recommended them to come forward to the Board for approval.

I want to point out that we still are well within the overall dollar amount. There was $76 million allotted for the broad for Cycle 2. If you approve both of these, we will still be well within that, at about $55 million.

The distribution between programs, which is done on an approximate formula, you can see over to the left, there is an approximate formula by which that is done, would be a little bit exceeded in the case of improving healthcare systems, so you would be going above its usual proportional allotment, but within the overall amount.

Those are the recommendations from the staff through the Selection Committee to add to the Cycle 2 2015 broad slate.

DR. NORQUIST: Christine, did you want to say anything from the Selection Committee?

DR. GOERTZ: No, I really don't have anything to add.

DR. NORQUIST: Sharon? Bob Zwolak?

DR. ZWOLAK: On the breast density study, there was an explanation in the agenda book of why

it fell out of cycle and what the extra requirements were. I didn't see anything about that. Could we have just a very brief summary of what negotiations or requirements pushed these two out of cycle?

DR. WHITLOCK: There were questions -- the first one, let me go back.

DR. NORQUIST: High intense periodic.

DR. WHITLOCK: The first one was the staff had been uncertain about it, and thought it might be worthy of an exception, but the SC asked for more detail, so we went back and filled in that detail. It was recommended to go forward. It was one in which -- that is what happened. Does that make sense, without getting into a lot of detail?

The SC asked us -- we had asked for an exception because we weren't sure that it made sense. We were asked to go back and confirm some things, and the SC felt it made sense to fund. It is consistent with another study that is funded by NIH in the younger age group, and we weren't certain that it made sense for the age group of children that it is being applied to, but through further

work, it seemed that it did, and so it is being recommended in score order.

DR. ZWOLAK: My question is focused on the justification for approval out of cycle. That is a perfect explanation.

DR. NORQUIST: The second one?

DR. WHITLOCK: The second one, I'm trying to recall. I believe this was one that was approved. Steve Clauser, are you on the phone? I believe this one was approved by the SC for further programmatic work, and we went and worked on it in the area the SC asked us to, and brought it back. It was approved and then brought forward. I believe that is how that happened. Sorry, I can't remember exactly.

DR. NORQUIST: Do you remember, Christine?

DR. GOERTZ: No.

DR. HOUTSMULLER: Hi, this is Elisabeth Houtsmuller. Steve Clauser is not on the phone, but I worked on this study as well.

DR. WHITLOCK: Thank you.

DR. HOUTSMULLER: That is what happened.

DR. WHITLOCK: Okay. When we were sent to work on it further, I can't remember what we were trying to get at, were we doing something with sample size or were we trying to get in an additional outcome about HCB transmission? I sort of recall that is what we were getting in as the issue of transmission. Is that right or no?

DR. HOUTSMULLER: Yes and no. We asked the investigator to extend the follow up from 12 weeks to 12 months, so that we could assess reinfection during that time, and because of that, we also asked him to increase the sample size, which he did, and a final question -- there was a question from the Selection Committee whether all the rural sites had broadband availability, and we checked on that, and they did. Those were the issues.

DR. WHITLOCK: Thank you. Yes, this has a tele-medicine component. Does that answer your question?

DR. NORQUIST: Yes. Any other questions or comments?

[No response.]

DR. NORQUIST: I need a motion to approve this.

M O T I O N

DR. ZWOLAK: So move.

DR. NORQUIST: Second?

MR. BECKER: Second.

DR. NORQUIST: All those in favor, raise your hand.

[Show of hands.]

DR. NORQUIST: Anyone opposed, raise your hand.

[No response.]

DR. NORQUIST: Anybody abstaining?

[No response.]

DR. NORQUIST: On the phone, Allen?

DR. DOUMA: Approve.

DR. NORQUIST: Harlan Weisman?

DR. WEISMAN: Approve.

DR. NORQUIST: Francis?

DR. COLLINS: Approve.

DR. NORQUIST: Okay. Thank you both very much. Our next one, we are going to have a

discussion of portfolio analysis, something we talked about in the past, looking at how we are doing in the areas of pain, sleep, I think that is really insomnia, and fatigue outcomes, as well as depression. Evelyn and Alicia?

DR. WHITLOCK: I am going to make this as quick as possible. This is a report back from the February retreat, where there was a discussion about the importance of measuring some key patient important outcomes, particularly commonly reported issues around mood, depression, anxiety, pain, sleep, fatigue.

With the help of the Evaluation and Analysis Group, we went back and looked at these outcomes across the portfolio. We looked across our portfolio data to look at projects that had at least one of the following outcomes around pain assessment or control, anxiety, depression, mood or well-being, and then coding for insomnia or sleep and fatigue.

The details are here, and I know you have those, so I won't belabor that. I just want to hit the high points here.

We did not look at methods projects, pilots, any of the projects that we were conducting in a co-funding kind of way through a Memorandum of Understanding with NIH or AHRQ or others. We didn't look at the PCORNet projects.

We did end up looking at 285 unique research projects, and out of those, about half, or 136, are reporting one or more of these outcomes related to pain, depression, or anxiety, sleep, and fatigue. Many of these report more than one outcome.

I'm going to show you a little bit of the descriptive statistics just so you get a sense of these outcomes across our portfolio and also how they are measured.

Going from Cycle 1 through spring 2015, 136 projects, you can see the most common of these patient important outcomes reported was depression or anxiety, and it was reported in 105 of the projects. Pain was the next most common, and then a few projects, 16 to 19, reported outcomes related to fatigue and sleep.

As you would expect, the number that reported these as primary outcomes was less than the number that reported them as secondary outcomes, and they are in about the same order of commonality as you would also expect from just their overall reporting.

We looked at what conditions they were in, because patient important outcomes don't necessarily just aggregate within single conditions. We counted each project once, so if for example, a project was looking at depression in cancer patients, if it was coded as the primary condition being cancer, then that is what was counted in this next series.

I'm also going to show you the measures associated with each of these outcomes, just as again an exploratory analysis, and as we look at the word clouds for the measurement instruments that are used, the larger the word cloud, the more commonly it was reported. This is just exploratory to see how commonly our awardees are using similar or disparate measurement approaches for the same outcomes.

This is really hard to read. I apologize for that. The big ones are easier to read. You can see from that the number of projects in the box, the number and type of condition are in the box, and that relates to the number of times the particular outcome was mentioned in that type of project.

For 105 projects that reported on depression or anxiety as an outcome, 20 of them were in mental or behavioral health kinds of conditions, which makes sense; 17 were in cancer conditions, and the next most common was cardiovascular health, and then neurological disorders.

You see there is a real array, so even in infectious diseases, depression or anxiety could be there or kidney diseases or other conditions, rare diseases, skin diseases, et cetera.

This shows these are reported across a number of different conditions with various frequency, and in terms of the instruments that are used, you can see that the PROMIS tools are used probably the most commonly, but many of the common instruments that were used through PHQ-9s and 8s,

there is a PHQ-4. From my systematic review viewpoint, there are many of these that we would have been able to figure out how to combine, but you also see there is some diversity across these.

Next are the conditions with pain as an outcome. In this case, the most common condition is neurological disorders that has pain as an outcome, followed by cancer and musculoskeletal disorders. Those make good sense.

A number of rare diseases address pain and then all the way across multiple conditions such as allergies and immune disorders, infectious diseases, et cetera. There is a range of conditions here as well.

I think the interesting part about the measurement tools is that the most common instance is the project design tool, and the second is the tool not specified, and down there a little bit smaller are the SF-36 and 12 and the PROMIS tools, and then a bunch of individual tools, some of which might actually be the same if you looked at it a little bit more closely.

This suggests we are not necessarily getting pain measures that would be combinable across the portfolio.

The next two are much less commonly reported, issues around fatigue and sleep. There is no scale between these. It looks it is very prominent here, but this might have been two instead of one. I couldn't get it to be scale across with the denominators, so I apologize for that. Similarly, a range of conditions with sleep, with again a range of measures.

The bottom-line from this, it was an interesting exercise. The SOC thought it was interesting and thought you would like to see it as well. What we concluded from it as an exploratory exercise is that patient important outcomes are commonly measured in the portfolio across different types of conditions or disease category.

There are variable measurement approaches, which could limit the synthesis of findings. For some outcomes, the most common tool was either non-specified or project defined, and it might be that

judicious use of core outcome sets could improve the coherence of PCORI's research portfolio and even its uptake if we focused on measures applicable to clinical practice.

I am happy to report that Alicia is going to be the discussant and she will entirely disagree with the point, so it will be interesting. Thank you.

DR. NORQUIST: All right, Alicia.

DR. WHITLOCK: Are there questions? Barbara?

DR. McNEIL: I have two questions, and I guess the first is probably for Gray. It strikes me that having depression or anxiety in only 20 out of the 105 mental health disorders, does that sound right to you? It seems a little low to me.

DR. NORQUIST: Depression/anxiety out of?

DR. McNEIL: If you go back a few slides.

DR. NORQUIST: I have to see what you are talking about.

DR. WHITLOCK: I know what you're talking about. I know where you are going, I'll go back.

Right there.

DR. McNEIL: Depression or anxiety as an outcome, 20 of them were mental health. Does that make sense?

DR. WHITLOCK: That was their primary condition, so remember I said some of these could have been like in cardiovascular health, say you are studying depression post-myocardial infarction, but the primary condition might have been cardiovascular, so this is partly how they are cataloged.

DR. NORQUIST: Now, it makes sense. Allen, do you have a question?

DR. DOUMA: Yes, could you explain the rationale for combining depression and anxiety in the same measure?

DR. WHITLOCK: I think that was actually done by the E&A folks, but I think it was easier because of the way the data are that you couldn't really separate them out very well, so you look at the variable definition, it is anxiety, depression, mood, or well-being of the patient or caregiver.

It seemed to be the best way to use the data in the way that they are currently coded.

DR. NORQUIST: Harlan?

DR. KRUMHOLZ: Thank you very much for surveying the portfolio for these important outcomes. I'm just going to go back, I feel obligated to continue to bring up my issue, which is how many of these studies are CER A versus B studies that we have been able to do rapidly, the benefit of providing people information about what works for them?

I still believe that all of these kind of outcomes, fatigue, depression, insomnia, pain, the list goes on and on, we fail to know what is the best combination of approaches are best for that person.

I would hope again PCORI in its last three years can find a way to do 100 studies that are randomizing alternative strategies to try to give us insight into which one of these strategies are best for which individuals.

It is useful to know these are being

collected, but I don't think many of them are in A versus B studies, the traditional CER that we are trying to do, and I think that is what we were really engaged to do at the inception.

I continue to think it is incredibly important for us to sprint towards a day when we can actually fund a wide range of these. I know we have the pragmatic program but I am talking about figuring out how we can become agile in moving forward in these kinds of studies.

It may be useful to standardize some of the outcomes for those domains, but even more importantly, I hope we can find a way to do a whole bunch of trials in this area with modest sample sizes because there are continuous outcomes and understand better what clusters of patients respond to which treatments.

DR. WHITLOCK: Do you think PCORNet is a good forum for those kinds of trials?

DR. KRUMHOLZ: Well, I think we invest a lot in that platform, that is one, but I wouldn't just necessarily restrict to that. I think it would

be great for us to hack this problem.

The question is how quickly can we generate knowledge in these areas knowing these trials -- what I want to do is let them compete, let others compete, see who can come up, let PCORI say we are looking for people to do these trials for us, by the time we are done -- we have heard from people that these are important outcomes.

I think we need to look at what are alternative strategies that are addressing these, what are top selling pharmaceuticals that are being used for these, for which the evidence is uncertain, and is one better than another.

In all of these areas, we have a whole lot of prescriptions being written to people and really inadequate knowledge about which ones are best for whom.

I think if we can contribute to that, that would just be terrific, and I know I'm interested in non-pharmacologic, too, but the pharmacologic is what is costing a lot of money, and I think we need to pay attention to that.

DR. NORQUIST: Alicia?

DR. FERNANDEZ: Let me make a few comments very briefly which I think synergizes perhaps with some of the things Harlan is saying. The first thing I thought when I saw this on the SOC is it is very interesting, and because the first thing to note is that these outcomes are either primary/secondary outcomes in about half of our studies.

When we think about the fact that we are a patient outcomes research institute, I don't know what the right number should be, but thinking that it should be around half, because mortality is also of interest to patients, morbidity is also of interest to patients, and lots of other outcomes, but to have these in around half of the studies is great.

I felt good about that, and we should acknowledge that or if people think it should be a higher or lower number, we should discuss that.

The second thing that I felt was interesting was depression was the outcome, either

the primary or secondary outcome in 77 percent of these. I also thought that was very good and appropriate.

The WHO lists depression as the number one in terms of robbing people of quality of life, and in the United States, I think it is a toss up between low back pain and depression, depending on which institute you ask. It is hard to overestimate the importance of depression, particularly as a co-traveler with so many other illnesses, and I was very glad to see the spread of illnesses.

That, Harlan, goes a little bit to your remark because for example, if in cancer we have treatment A, you know, oncology cocktail 1 versus treatment B, oncology cocktail 2, depression may very well be an appropriate outcome that should be measured and that we are not actually looking obviously at pharmaceutical treatment for depression.

The third point I wanted to make was around the metrics. When I looked at the metrics, I had some concern, as I think probably all of us would,

around not defined, and I just think go back to it wasn't very many.

I don't know exactly how many, but it didn't seem to be very prominent, but again, I don't understand how you could have a primary or secondary outcome that is not defined that gets through merit review, so I'm hoping that will be solved or I'm hoping that represents small numbers.

DR. KRUMHOLZ: Does that mean that wasn't a standardized -- for clarification, does that mean there wasn't a standardized instrument?

DR. FERNANDEZ: It wasn't defined apparently.

DR. WHITLOCK: These data come from the research plan, so we also have to consider the data source.

DR. FERNANDEZ: On the other hand, I was very happy to see the instruments that were there, and in particular I want to call out the use of the PROMIS instruments. Some of you may be less familiar with this.

This is a very large, very important NIH

initiative. It stands for Patient Reported Outcomes Measurement Information System. It is a data bank of items, and you can select them, and they have been validated across not only different populations of illnesses, but across the general population. Many of them are available in as many as 40 languages.

What is the point of being happy that our researchers are using them? It does allow us to do standardization and systemization if we wanted to across different illnesses, and also benchmark against the general population.

All and all, I felt very content to see the data that Evelyn and the team pulled together. We have a small measure, I wouldn't even say disagreement, but it has to do with how much should we be investing in making everyone use the same, going backward, and making everyone use the same data outputs in terms to facilitate systematic review.

I tend to think there are a lot of opportunity costs associated with that, and I would

rather see us sort of continue with a very sharp eye to make sure everyone is using obviously one of the more popular measures.

Finally, picking up on what our specialty colleagues said today about wanting us to maybe put in some funding into psychometrics or into other patient reported outcomes, I do think this is an area where we can explore with NIH, because that really is what PROMIS does.

Now, for example, I was just looking on their Web site, they have PROMIS for GI diseases, and it relates to GI symptoms. Perhaps there could be a PROMIS respiratory, and someone can figure out how to ask about breathlessness in a way that we are confident around patients' answers.

That is it.

DR. NORQUIST: Thank you, Alicia. The only thing I would say on the measures is also not just with NIH but also with other organizations. In psychiatry, we are very interested in measures being used for depression. I think it is key that we interface with all the relevant groups.

The reason the PHQ-9 is so high on that particular one is that is the one the APA and others are pushing right now.

DR. FERNANDEZ: That is the one what?

DR. NORQUIST: The APA, the PHQ-9 comes out pretty high on that.

DR. FERNANDEZ: Right. For example, PHQ-9, we actually use in clinical practice now. It has gone from being a research tool only to a clinical tool, whereas I don't believe PROMIS -- I don't know that any of the PROMIS instruments are used in clinical practice, they are too cumbersome.

DR. NORQUIST: Right.

DR. FERNANDEZ: You could certainly see why one group would choose one versus the other. I'll stop there. I think this was an encouraging exercise.

DR. NORQUIST: Other comments? On the phone? Francis?

DR. COLLINS: I appreciate the shout out about PROMIS, which has been a work in progress now for I think about 11 years at NIH, building off this

set of validated questions, which I think has turned out to be really valuable for lots of clinical research, but may not be perfect for things like depression.

I guess the message I would take from this is we do have a really serious interest in making sure we can do comparisons across studies if possible, so maybe what we don't want, unless we are talking about a very specialized situation, is for an investigator to start from scratch and come up with an entirely new way of assessing patient reported outcomes when there are already well designed and well validated alternatives they could use. If that message could reach sort of the next round of reviews, that might be a good thing.

DR. NORQUIST: I think that is a very good point. I think it should be clear, they shouldn't be coming up with totally new things and they should certainly make a rationale for why they picked the measure they are picking also.

Other comments?

DR. WEISMAN: As just has been said,

validated instruments for patient reported outcomes, how many do we believe are patient-centered patient reported outcomes?

In other words, the outcomes that are being measured are meaningful and understood by the people being measured, whether they are the parents of children and reflecting their concerns about their children or adults who have diseases.

DR. FERNANDEZ: The instrument that I'm most familiar with is the PHQ-9, mainly because we use it in clinical practice as well as research. I have certainly looked at the Spanish version and it includes cognitive testing, and it includes other measures to make sure people are answering them appropriately, whether every patient identifies all nine symptoms as related to what they would consider their depression is certainly not the case.

The PHQ-9 and PROMIS tool may be certainly the best depression inventory. These are instruments that have been cognitively tested in diverse populations.

DR. NORQUIST: They have been widely tested

both in various racial and ethnic groups and income levels as well.

DR. WEISMAN: I'm not questioning that. I'm questioning whether can they provide useful information to the investigators and maybe clinicians in some way, but are they only measuring the things that matter most, that they measure across demographic and other characteristics, whether they are measuring what is important to the patient.

DR. NORQUIST: In answer to your question, particularly in depression, I think the sense of depression is important to a person, and that is what we are measuring. There are a variety of other things that go along with that that may differ across patients, and that is where other things come in.

As psychiatrists, we use this as an indicator of where we sit, but it is not the final measure of when we make a determination and what we are doing with the person and how improved they are.

Leah?

MS. HOLE-MARSHALL: I thought we had as a methods standard that it was required that outcomes be identified, so I don't know how we could get to a tool not specified, especially, but even the project design tool, we want validated instruments.

I agree with your general comments, Alicia, that this was a great review and there is a lot of good things here, but those ones pop up fairly regularly, and it is concerning, somewhere in between mandating you can only use one or two tools to we have a guesstimate of this word cloud as 45 tools, and that doesn't account for each project tool, you would have to add the numbers.

There is probably some happy medium in there that we can continue to refine our PFAs or our methodology standards to be more specific, given that our tradeoffs are no one of these studies is likely to change practice, so it has to be combined in order to have power, and we are not going to be able to do it if we are not moving in the direction of more validated tools.

In addition to the combo issue is just if

it's not validated, what do we do with the results, the tool itself is not validated.

DR. NORQUIST: I assume we are using validated. Robin?

DR. NEWHOUSE: The discussion was going in the direction of my comment, but yes, the methodology standards do include the need for psychometrics, and patients identifying the outcomes that are most important to them.

I think the other thing that struck me was on the pain measures, the incidence of project design tools, particularly since a lot of our discussion was around pain and pain management and opioids, the importance of having a psychometrically sound tool is incredible.

Of all the portfolio that you presented , it was the one that was most surprising to me, and just wondering, we are not funding psychometric studies, so there must be some criteria that would require, because you didn't look at the methods, so I would imagine they would be in that portfolio.

There would have to be some requirement

that the investigators report when they design their own instrument so that we understand and can believe there is reliability and validity.

DR. WHITLOCK: Of course, I wasn't here for any of this, but what I would say is a couple of things. These data come from the research plans. They are not from the protocols. So, we have to consider that before we make binding conclusions about what is going on, I think this raises questions, we would need to look at the research protocols and be sure that the tools not specified or the project design tools are indeed those.

You raised the exact point that I thought, especially across pain, it seems like we ought to be able to have -- that is an area if I was going to work on one of these areas first, I would probably start with that measure.

DR. NORQUIST: That one seems to be the one with the most differences and one that is critical particularly as we go forward looking at opioid use and stuff.

DR. FERNANDEZ: I didn't necessarily

support going backward and asking people to sort of redo their work, I do think for the studies that we have going forward, it might be very helpful if we could suggest that people use one or two measures or whatever the right number is so we could actually get some synergy across.

I also think this can be addressed in multiple places, in the application process, not the least of which is at merit review.

DR. NORQUIST: Andy?

DR. BINDMAN: Hi. First of all, this is great to see this analysis, thank you for it. I was just wondering what the mechanism was that you anticipated being able to
-- to pick up on what you are saying, the notion of why some of these things are going on, and what the feedback loop is to us about why some investigators may have made choices.

I think there is sort of an implicitness that maybe people aren't choosing these valid instruments because they don't know about them, but I wonder if there are other barriers that are

preventing them.

I know in my own experience of supervising trainees, sometimes they run into IRB challenges with some of the tools. This is the issue that sometimes comes up with the PHQ-9, with the suicide question, and the ability to be able to do follow up if patients respond to that or participants respond to that, and need to have that in place.

I just wonder if there are other barriers that are preventing the use of what looks valid scientifically from being able to use some of these patient reported outcome tools, and more importantly, what feedback or mechanism we have to be able to identify why maybe they are not being used.

I fully endorse the notion of trying to standardize it, but I want to make sure there isn't some implementation problem that we are not anticipating by just saying oh, they must have missed the fact that there is a tool out there. My guess is there is more to it than that.

DR. WHITLOCK: I think the other issue here

is there may be multiple outcomes per study, so for example, if you look at some of the PFAs and things that we put out, there is a lot of outcomes, both primary and secondary. There may be multiple tools per study. I don't have the ability to look at that through these data. We didn't look at it that kind of way.

I think it would be hard -- first of all, we would have to confirm -- these are from research plans. We would have to look at protocols as a second round, as these are kind of hypothesis generating, and it looks like people aren't using validated tools.

Second, I think we would have to say across projects, do they have one validated outcome, and then they have a variety of other measures that are perhaps not validated because they engaged a lot of folks and got a range of outcomes. That would be a second question.

I think we don’t know, and third, is there something that ought to be picked up earlier in the process, merit review or is it the fact like you

were saying, is it because people don't know, do we need to produce a list. I don't really know.

I think the first thing to know is do we have a problem, and we would have to look a little more closely at this to see how well the research plan data are confirmed by protocols.

DR. NORQUIST: Other comments?

[No response.]

DR. NORQUIST: Many of these are linked together. I see people with pain who have depression, insomnia, anxiety. They all go together. Thank you very much. Thank you, Alicia, for looking over this.

As no one is present or waiting on the line, we will not be initiating our public comment period. We always welcome your feedback at Info@PCORI.org or through our Web site at PCORI.org. Not surprising because we have so many other avenues now for input that we don't have this. Andy, in the early days, we had people in the room and stuff, now we have so many people online.

We are not going to wrap up just yet

because this is Steve Lipstein's last in-person meeting with us. Unbelievable as that is.

[Applause.]

DR. NORQUIST: Also, Harlan Weisman, this is his last, but he is not in person, I should say, because Harlan is on the phone. We also want to thank Harlan. Now, you don't get off the hook either one of you because you still have a service through September, and so you will get your wonderful plaque and fake check and all that stuff at that point.

I want to thank both of you. It's not real because we don't have any money to give. Steve, in particular, for those of you who are relatively new, he and Jean basically almost in the basement, in fact, out of their garage, started this thing, handling extra large checks into Jean's bank account. You never finished the story about who actually paid the IRS. That is why he went to North Carolina. No.

We better be quiet or we really are going to get in trouble. Anyway, for those of you who are

going to join us for dinner, we will be having a celebration. Harlan, we will have to celebrate you, maybe we will record it or something.

Thank you, Steve, very much. We have really appreciated your service, and Harlan, too, your service.

Let me close by thanking those who joined us today, both in person and via webinar and teleconference, and a reminder, all materials are available on our Web site. Our webinar was recorded and will be probably posted by the end of the week, and we always welcome your feedback on our Web site or at Info@PCORI.org.

Thanks, and good evening to everybody. Thanks.

[Whereupon, at 5:24 p.m., the meeting was adjourned.]