PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

BOARD OF GOVERNORS MEETING

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Almas Shriners Building
1315 K Street, N.W.
Washington, DC 20005

[Transcribed from PCORI teleconference.]

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Barbara McNeil, MD. PhD
Grayson Norquist, MD, MSPH [Chair]
Ellen Sigal, PhD
Harlan Weisman, MD [via telephone]
Robert Zwolak, MD, PhD

AGENDA

AGENDA [Continued]

P R O C E E D I N G S

[10:15 a.m.]

CHAIRMAN NORQUIST: Good morning. I'm Dr. Gray Norquist, Chair of the PCORI Board of Governors. I want to welcome everyone to today's Board meeting, which we are holding in person in Washington, D.C., as well as via teleconference and webinar.

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

All Board members are present with the following exceptions, Allen Douma, Freda Lewis-Hall, and Harlan Weisman are participating via phone. Steve Lipstein is absent and Francis Collins is out from 10:00 until about 12:30 p.m. Eastern Time.

I want to remind everyone that disclosures of conflicts of interest of members of the Board are publicly available on our website and are required to be updated annually.

Members of the Board 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 will deliberate or take action on a matter, which we will today, that presents a conflict of interest for you, please inform me so we can discuss how to address the issue. If you have questions about conflict of interest disclosures or recusals relating to you or others, please contact your staff representative.

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

We have scheduled a public comment period today from 5:30 to 6:00 p.m. Eastern Daylight Time. If you are interested in registering to provide public comment, please visit our event page for instructions, or you can always e-mail us at Info@PCORI.org or provide input through our website, PCORI.org.

A final reminder, we are live tweeting today's activities on Tweeter, and you can join the conversation at #PCORI.

The first item, I am going to introduce Joe Selby, our Executive Director, who wants to provide a few brief introductory remarks.

DR. SELBY: Thank you, Gray. Good morning, everyone. I want to start by advancing my slide. I want to start by noting that five years ago last week, PCORI's first Board of Governors was named by the GAO. I wanted to take a moment to congratulate the Board and to thank the Board for having stuck with this amazing adventure, this experiment, for five years.

We have had three people leave the Board in five years, 18 are still with us. Two of the three people who left actually left because they had to, simply because their jobs changed. One took a job with the Government which meant he had to leave, and one left a job with the Government, which means as an ex officio member, she had to leave. An amazing record.

At PCORI among the staff, I know I often wonder and wish I could have been here for that first Board meeting. You got handed a lengthy document. You were besieged by stakeholders from every corner of the country telling you that they had helped write the legislation and this is what it really meant. Out of that, you made a very consistent organization that we are all proud to be part of.

I went to the PCORI website last night because I thought maybe that very first meeting was archived. We have most of the Board meetings archived as either webcasts or now webinars and recordings. I just wanted to hear the tone in people's voices the first time they laid eyes on each other and tried to tell each other what they thought PCORI was going to be about. Unfortunately, we didn't archive them quite back to the beginning.

MS. GOERTZ: None of us would be willing to take notes. That's why.

[Laughter.]

DR. SELBY: I thought if I could have found that one, I would have put a little bit of it up this morning for you.

At any rate, just to say that we really appreciate your endurance, your patience, your hard work, your thinking. We have come a long way. I think you will agree this last year particularly has been just a really special year of getting things better. Staff, we call this the "year of the tweak," because we are just improving everything that we do.

We are moving rapidly toward having study results. You are going to see three exciting study results, and towards having approaches that we are all very proud of for culling out the topics, the research topics, of most interest to stakeholders and getting them funded.

Thanks once again. We will move on from here.

CHAIRMAN NORQUIST: Thanks, Joe. The next agenda item is the Consent Agenda. Do we have a slide for that? That is not the Consent Agenda.

We need to approve the minutes from the August 18 teleconference Board meeting. The second one is approve the nomination for the Governance Committee, Robin Newhouse, to serve as chair, and Steve Goodman to serve as vice-chair of the Methodology Committee for a second term.

UNIDENTIFIED: I move approval.

CHAIRMAN NORQUIST: Any discussion about either one of these items?

DR. SELBY: I think we should include a thanks to both of them for their remarkable service.

CHAIRMAN NORQUIST: Yes, thanks for their remarkable service and willingness to continue on. Thank you, Robin. Robin is sitting here.

No discussion. I think we can do this simply by a voice vote. All those in favor?

[Chorus of ayes.]

CHAIRMAN NORQUIST: Anybody opposed?

[No response.]

CHAIRMAN NORQUIST: Anybody abstaining? That goes for people on the phone, too.

[No response.]

CHAIRMAN NORQUIST: Okay. Thanks. Next up is your report, Joe.

DR. SELBY: Speaking of time passing and movement, as I think the Board knows, we are at a juncture in the life of the CSO at PCORI. Bryan Luce, who took this job in late 2013, it was a daunting job when he took it because there was obviously so much to be done in terms of figuring out how in the world we're going to get to targeted approaches to funding CER, how we are going to manage this portfolio, and mainly how we are going to recruit and grow and train a staff, create a culture for doing science at PCORI.

Bryan approached it with a degree of energy and intelligence, enthusiasm, and he believed, I think, like I believe, that research is about the most fun thing you can do and get paid. He conveyed that throughout his time with us, two plus years. He did it all with a real classy gentlemanly approach that I certainly learned from and I think we all did.

His whole career has really been looking at outcomes, looking at value, applying reason and science to improving health services, allocations, and helping patients make personal decisions.

I want to thank Bryan now, but I want to say also that Bryan is going to do his duties here today one last time. Everybody in the room and those on the phone will get to hear his dulcet tones once more as he brings the most recent slate and some new topics to the Board.

I asked Bryan if he wanted to say a few words now, and he will make some comments when his time on the agenda comes. I want to just personally say to Bryan, wherever he is sitting right now, what a joy it has been to have him with us, how much he has advanced PCORI's course, and also to say he will be with us on a part time consulting basis to help particularly in building and strengthening PCORnet's ties to industry, to life sciences industry, and also in some of the angles of methods, particularly for things like adaptive trials.

I will stop there. Christine?

MS. GOERTZ: Thank you. Bryan, I just wanted to also thank you for your work. I don't think there is anyone that is more committed to PCORI's mission than you have been, both in your time before PCORI, your time during PCORI, and I suspect your time after PCORI.

I will never forget the first time I got to meet with you, you actually demonstrated that commitment early on by being the only person associated with PCORI that actually has traveled to Davenport, Iowa, came and met with me there. I was really impressed with your passion and your commitment. I have had the chance to work with you very closely over the last couple of years.

A couple of things in addition to what Joe has said is the way you are able to inspire loyalty among the people that work for you, it has really been something that has been a real pleasure for me. I have learned a great deal from you, in watching how you make that happen. The last thing I'd like to say is probably one of the most

important qualities that a person can have is to be kind. You have that combination of a commitment to our mission and are truly kind.

Thank you. I have enjoyed working with you.

DR. SELBY: Keeping with the theme of moving forward, Evelyn Whitlock is here. I think many of you might have met her at breakfast already, but I will ask Evelyn to stand.

Evelyn comes to us from the Center for Health Research and Senior Director of the Evidence-Based Practice Center for Kaiser Permanente Northwest. This is one of AHRQ's evidence-based practice centers.

Evelyn is really a national leader in the application of evidence synthesis to decision making and policy making. She's done just hundreds of evidence syntheses for the U.S. Preventive Services Task Force, and also numerous evidence syntheses in her work with the DEcIDE network and through the Evidence-Based Practice Center.

I think at this time when we have a large

portfolio of projects that we have to manage well and in fact synthesize, where we are really moving to an industrial strength version of topic generation and development of topic briefs on questions stakeholders have brought to us, it's exciting to have somebody who as she said has this framework of evidence synthesis as the way she approaches questions.

I think it is very complimentary to the people that we have at PCORI already, and very fitting time-wise. I really look forward to Evelyn's arrival, which will be in January of 2016. She will also join us for dinner tonight, so you will get to know her a little bit better.

I want to thank the Search Committee. We had a very vigorous search, a very vigorous national search, with a lot of interviews, a lot of candidates, a lot of time, and both the Board members and staff members who participated on the Search Committee really did great work. We are really grateful. I think to a person, the Search Committee felt like we got the right candidate for

this position with Evelyn. So, welcome, Evelyn.

I mentioned that time is moving along and we now have results. I just want to say again to those of you on the Board, this is just an example, there are several of these on the Board now, reports and results from important studies. If you go to the PCORI website, you will find it. If you go under Research and Results, you look for PCORI in the literature, and you will find well over 30 publications from PCORI funded studies.

Very exciting. I was just looking through them yesterday and wound up reading a few of them. It's going to be tough to keep track of all this but our website does a very good job. I commend it to the Board members as sort of a way to keep up to date with what we are doing.

I also want to take a minute to celebrate a new and big award which comes to us by way of a collaboration between PCORI's Addressing Disparities Research Program, led by Romana, and the NIH, specifically NLHBI and NINDS, two of the large institutes there.

Very successful collaboration which led to a funding announcement for comparative effectiveness studies, testing multi-level, multi-component interventions aimed at reducing hypertension disparities, improving hypertension control in racial and ethnic minorities in low SES populations and/or rural populations. A total commitment of $23.5 million. This is administered through NHLBI, I believe. In every way, it is collaboratively managed.

The two awards are for Dr. Safford, University of Alabama, for a collaboration for improving blood pressure control in what is called the “black belt,” geographically the highest stroke incidence area in the country, and it compares a very rigorous CER study comparing two approaches for supporting primary care practices in managing hypertension in this population, and Dr. Lisa Cooper at Johns Hopkins for a study that focuses on the State of Maryland, both urban and rural areas in the State of Maryland, again comparing a rigorous CER study comparing two approaches to

supporting primary care practices in managing hypertension.

I think most of you know our first annual meeting, the meeting that the Board has been calling for since 2012, is actually taking place next week here in Arlington. We are anticipating an attendance of over 1,000 of the PCORI community. Many of them are funded investigators. Many of them are patients and stakeholders that are affiliated with PCORI, either through the funded research or in other ways.

The meeting is dedicated to several critical topics, including dissemination. The first half-day is a joint meeting with AHRQ. Academy Health facilitates the meeting. AHRQ and PCORI are and have been in the process of figuring out how we listen to the PCORI legislation and make certain we are prepared to disseminate the findings of PCOR research, particularly that funded by PCORI, but other critical research as well.

That first half-day is a joint AHRQ/PCORI meeting dedicated to dissemination. The panels

that afternoon are remarkable. They start with a keynote by Mark McClellan after some introductory remarks by Gene Washington. Gene will then be a panelist that afternoon as well. I think that will be an interesting afternoon.

The next day, Wednesday, we have a state of PCOR keynote address by Dr. Victor Montori from Mayo Clinic, and then an entire day of presentations of the research that we have funded, organized by topic so you will see synthesis of research findings in action that day. Very exciting.

The next day, we are really fortunate to have Francis Collins kick off a really interesting forum on open science. Francis is the lead. The moderator is Austin Frakt, otherwise known as the "Incidental Economist," and a group of panelists, a really exciting group of panelists will round that out, after which there are a number of summits of various groups of researchers funded by PCORI for the rest of Thursday. A great day.

Any number, and I don't have the exact

number, but a number of you are signed up to play roles either on panels or as moderators, and I thank you all for your interest in the meeting and willing to play that leadership role.

I will stop and see if there are any questions about anything we have said so far today.

DR. ZWOLAK: Bob Zwolak, Board Member. Thanks. That was a great initial presentation. I was wondering if you could provide a tiny bit of detail about the $23.5 million collaborative project with NIH for hypertension and in particular to the management. We do contracts. NIH, I think, does grants. Is this a grant or contract? Is this a model of collaboration? Have you worked out the details of who is going to be managing this and how the collaborative approach will work? Thank you.

DR. SELBY: I think I will ask Dr. Hasnain-Wynia if she wouldn't mind answering that. She has more details than I do.

UNIDENTIFIED: Joe, while she is coming up, for the annual meeting, will any of those sessions be webcast?

DR. SELBY: Yes. My impression is all the general sessions are webcast. Correct me if I'm wrong. Hi, do you need me to repeat the question?

DR. HASNAIN-WYNIA: No, I heard the question. Thanks. This has really been a great collaboration, and it was a collaboration from the very beginning, from the development of the funding announcement, and will follow through the implementation and management of the trials.

The monies were delivered to NIH from PCORI. NHLBI is the organization at the NIH that is primarily responsible for managing the trials. PCORI representation is on the Steering Committee. We are managing and monitoring the milestones with NIH.

The other piece of this that I think is very important is this is a cooperative agreement, not a contract, not a grant, something in between. We are implementing an UH2/UH3 model, which means after the first phase of the trials, we will review the milestones and determine whether the second half of funding will be delivered to each of the

awardees. We have instituted a way to make sure that PCORI is very engaged and truly collaborating with NIH in terms of the management of these trials.

DR. KRONICK: Thanks. I am very excited about this. It sounds like you have laid all the ground work to make it work well.

DR. HASNAIN-WYNIA: Thank you.

CHAIRMAN NORQUIST: Harlan?

DR. KRUMHOLZ: First, I also wanted to thank Bryan because his work has really been remarkable in a period of challenge, and his contributions to PCORI are much appreciated.

Joe, I just want to ask about the meeting. Is there any news that is going to come out at the meeting or are you thinking there is any messaging for the press?

Is your goal more just around building the community, which is a wonderful goal, but in anticipation for the Board, I was just wondering if there is anything that is going to be released or if you have some top lines you want people to pick

up on, and is this something we are billing as something we think the press will pick up on, or is it really just more an inside PCORI kind of event?

DR. SELBY: I think we have been thinking of it as a building the PCOR community, explaining to the public much more about AHRQ's and PCORI's joint mission in dissemination. I don't think we see it as any new news. There is not going to be any new news.

The keynote, I think, will really be an update to the country and to the research and patient communities on PCOR and PCORI at five years. The open science will really hope to make some progress in this difficult area, particularly make some progress in pointing to ways that PCORI can participate.

I think if there is any new news, one thing is this will be a little more blatant, I think, than we have been about PCORI's intentions around open science. I think that is one area that we really haven't discussed much at Board meetings to date or in committees.

DR. KRUMHOLZ: When will that be most evident in the meeting?

DR. SELBY: Thursday morning.

CHAIRMAN NORQUIST: We are ready for the Dashboard.

DR. SELBY: We are ready and with immense thanks as always to Michele Orza and to the whole team, the evaluation and analysis team, and also to Regina and the whole administration/operations group, and to science, to engagement. Everybody now participates in this Dashboard, and for people like Harlan Weisman, who I think is not with us today --

CHAIRMAN NORQUIST: He's not on the phone?

DR. SELBY: I haven't heard him.

CHAIRMAN NORQUIST: Harlan, are you on the phone?

[No response.]

DR. SELBY: It's a holiday, religious holiday. The real news is this Dashboard lays on top of Dashboards in various sectors of PCORI. As always, we look to you to give us suggestions for

evolving it further and making the information more useful.

Today we are going to focus on four areas. I will do three of them. I will do an update at the top. We always have stories about the impact of PCORI. I will address one of the two yellow areas, the funds committed to research, because you will see there is somewhat of a deficit. This is the Dashboard through the third quarter, so since we are now through the fourth quarter with three days to spare, you have to remind yourself this is really through the end of July.

Also, on the upper right, I will talk to you a bit about improvements and evolution of our measures, of how our funded projects are progressing. The one on the bottom, the budget for 2016 and the shortfall of expenditures in 2015, will be taken up in the next agenda item, which is the budget. Regina will join me and Larry from the FAC in presenting this.

Let’s go to the very top item, the interesting and useful information, which is

producing that is our main mission. I want to show you the results of three published studies that really exemplify three of the distinctive features of patient-centered outcomes research or comparative clinical effectiveness research PCORI style.

One study is just a classic illustration of how we weigh the benefits and the harms of alternative choices to treatment to help patients and clinicians make decisions. The second is a very patient-centered aspect which is individualized prediction of who will benefit, what works for whom. Treatments may look like they work on average but that average can hide real differences in who benefits and who doesn't benefit and may even be harmed. The third is what happens when you really put patients on the research team.

These are three studies. You have heard a bit about this study. This is Dr. Ron Keren from CHOP, the pediatrics hospital in Philadelphia, comparative effectiveness of using intravenous antibiotics delivered through a catheter that goes

right onto the heart versus oral antibiotics in children when they go home after a serious bacterial infection. In this case, an infection called osteomyelitis.

They are actually doing three studies and this was the first one to be published. Their award is not finished yet. The results, which were published in JAMA Pediatrics at the very end of last year, showed that antibiotic therapy delivered orally versus that delivered with a PICC line or this intravenous line were equally effective for curing the primary infection.

The PICC lines, as people have known for years, were associated with a 16 percent incidence of severe adverse events, events like infections, clots, even a catheter breaking off, that occasioned kids coming back at least to the emergency room and many of them being re-hospitalized.

They also looked in stratified analysis. They were particularly concerned that oral antibiotics may not be as good in younger children

or those with MRSA infections, but oral antibiotics had the same benefit in those younger children, those with MRSA infections.

To quote the authors, "We found no advantage of the more invasive PICC route. Given the magnitude and gravity of the PICC related complications, clinicians should reconsider prolonged I.V. therapy when an effective oral alternative exists." I am going to come back to this study in a minute.

This is a study that illustrates individualized prediction of benefit, what works for whom. This comes from Jeremy Sussman at the University of Michigan and David Kent from Tufts in Boston.

This was basically a pilot project, a reanalysis of the DPP, diabetes prevention program, which was a large randomized trial that showed both lifestyle interventions and the use of a drug called Metformin, could remarkably lower the risk for developing Type 2 diabetes in persons who were judged to be at increased risk for developing type

2 diabetes. It is an intervention to prevent the development of Type 2 diabetes.

The average results across the whole population were that both Metformin and lifestyle interventions were beneficial. Lifestyle interventions were somewhat more beneficial than Metformin. Metformin still reduced risk by about 38 percent, which is big.

The results of this analysis broke this group of high risk people into four quarters, and the four quarters were four quarters of risk, so among higher risk people, there are some that are nearly diabetic, they are at the highest risk, and others graded at lower risk across the four quarters.

What they found is the benefits of Metformin were almost exclusively confined to patients in that highest quarter of risk, so people who were almost diabetic already, Metformin helped them. There was absolutely no benefit, in fact, it appeared there might even be a little harm in the lowest quarter. These are high-risk patients but

they were at the lowest quarter of the high risk patients. By contrast, the lifestyle intervention gave meaningful protection, sizeable protection, in all four quarters of risk.

Barbara?

DR. McNEIL: I don't remember that study to be honest.

DR. SELBY: DPP?

DR. McNEIL: No, I remember the DPP. I don't remember this reanalysis.

DR. SELBY: This is pretty new.

DR. McNEIL: Does this mean they were actually giving Metformin to people with normal blood sugars?

DR. SELBY: "Normal" is a strong word.

DR. McNEIL: Under 125.

DR. SELBY: Yes, absolutely. Metformin, in fact, it has crept into practice for people with impaired glucose tolerance, quite a bit of it is used. This study says you will do much better with lifestyle unless you are maybe with a fasting glucose of 118 to 125. In the other three

quartiles, you should be focusing and you will get more benefit from the lifestyle.

Their conclusion was patients at high risk for diabetes have substantial variation in their likelihood of benefitting from various diabetes prevention treatments. Using this knowledge could decrease over treatment. That is over treatment with Metformin, and make prevention of diabetes more efficient, effective, and patient-centered. Very nice individualized prediction.

The third one is Dr. Adrian Hernandez from Duke, involved elderly patients in a prospective observational study of the real world effectiveness of using Warfarin after patients have had an ischemic stroke who are also found to have atrial fibrillation.

We know in younger people Warfarin dramatically lowers the risk of stroke in people with atrial fibrillation. We did not have good evidence about older persons, people who had a stroke already and whether the benefits of Warfarin really outweighed the risks of Warfarin, this blood

thinner, in these elderly patients who had many comorbidities.

They are actually doing three studies, antidepressants and statins are also being investigated. They involve patients -- the patients said we really don't like the outcome of mortality and we don't like the outcome of recurrent stroke, they are just not of that much interest to us, but what we really care about is the amount of time we are able to spend at home.

This study shifted the main outcome to days spent at home during follow up. Probably the first large outcome study to use this as an endpoint. They also had quality of life. They did have mortality. They had all cause readmission and disease specific readmission. What they found was in a cohort of 12,500 patients with atrial fibrillation, post stroke, those that were started on Warfarin before discharge enjoyed 47 more days. That is almost seven weeks, more days at home, during up to two years of follow up, as well as lower rates of recurrent stroke and death.

These findings, I think, as the author said, support the routine use of Warfarin for eligible ischemic stroke patients with atrial fibrillation, including those over 80 years of age, women, those who have had more severe strokes, and those with comorbid conditions.

I think the findings from this study become easier to communicate to patients, that use of this drug has been associated with a much greater number of days spent at home during follow up.

Those are three studies. Back to the first study. Yes?

MS. HUNT: I know there is also these new drugs that are like Warfarin that are newer than Warfarin. Has there been any head to head comparison on this topic with those new drugs and Warfarin?

DR. SELBY: I don't think there has been a head to head comparison yet in this particular population of 80+ year old people who have had a stroke. There have been a number of head to head

comparisons.

I will remind you we approved a targeted funding announcement in this area, including a head to head comparison of the new agents. I don't think we have a comparison with Warfarin. I don't believe we do. Barbara? BMJ. The first one was in JAMA Pediatrics and the last two were in BMJ, British Medical Journal.

Speaking now about disseminations. When we saw the results of the Keren study about the PICC lines, we worked with the American Academy of Pediatrics and with a firm that does continuing medical education and continuing education for non-physician professionals. That was launched in mid-June. It is a web-based video program targeted to physicians, physician assistants, nurse practitioners, pharmacists, nurses, care managers, and health education specialists.

It has been up and running for three months through the summer. The vertical bars on the right show you the number of CME or continuing education certificates that have been issued thus

far. Our first dissemination activity, if you will. It was launched very quickly, as I think these will have to be.

This is just an example of tracking the use of information, so Altmetric is like the Science Citation Index, but it goes into a little more detail. It reported that this paper, Ron Keren's paper, has been in the top five percent of all the articles they have scored. They have scored four million articles to date. It is in the top five percent, almost 10,000 total views, 7,000 page views, and 2,784 PDF downloads.

Lastly, Dr. Keren reports to us that the Pediatric Infectious Diseases Society is preparing a new practice guideline on bone and joint infections in children, and will consider the findings of this PCORI study in developing its recommendations. It is what we like to see, that useful research has been taken up and considered by guidelines developers.

One other nice piece of news, this is not a publication, but this comes from the University

of Texas Health Science Center, San Antonio. PCORI is credited by the Assistant Dean for Research in Student Programs with motivating workshops that the university has held on PCORI that led to development of a listserv working group focused on developing PCORI applications with about 130 investigators participating, and a day long in-service on grant writing. KickStart or CLIK awards, $50,000 to new investigators who are preparing patient-centered outcomes research proposals, and particularly to fund meaningful engagement with partners, patients, and others.

New policies also at the university, and this has to happen at a lot of universities to allow the hiring of patient or stakeholder partners as experts on the university's payroll.

Patient-centered approaches to applications for research to other funders.

Just all the kind of things we like to see, UT, San Antonio has reported what is going on there. One of the Chiefs of Community Recovery, Research and Training said PCORI's approach has

changed everything about the way the university thinks about research, a ripple effect that would not have been anticipated.

I am going to go now to a blow up of that first yellow box which shows through three quarters, we are somewhat underspent. There has been a lot of spending. "Underspent" is the wrong word. Under committed. This is about committing funds for new research. We will commit a lot of funds. We did, I believe. PCORnet has already gone through and some pragmatic clinical studies were approved at our last Board meeting which was in the fourth quarter, and we will approve a slate of broad funding announcements and a slate of Hepatitis C targeted proposals today.

We will have a large amount of commitment in quarter four, but we will not commit as much as we had proposed, which was over $600 million, in 2015.

Based on discussions at the last Board meeting, we have launched a large number of inquiries, mostly through the SOC. You are going

to hear later today from Lori and Laura from our Evaluation and Analysis group about some of the work and some of the data collection and analysis we have done in the application enhancement group.

We are looking at everything from the applications, from what scientists say, to what about scientists that aren't applying to PCORI, and also into the merit review process, for ways to enhance the number of applications and the number of high quality applications that we get.

This just shows you that really the shortfall is not in the targeted. We do well, and we actually have overfunded slightly compared to what we said. In the broad's and in the pragmatics, when we tell you what our target is, it is a function of adding several, up to $56 million, up to $90 million, up to $30 million, and any time that any cycle falls short of that, it sort of contributes to the overall shortfall.

You will see particularly in the pragmatic studies, which is a surprise to us, we have not been able to fund as many as we thought we would.

You will see more of that this afternoon. We will continue talking about this. This is part of the tweaking activities in 2015 and into 2016.

Now I want to talk a bit about measuring the progress of research budgets. You have seen this for several months. I am going to just take you from left to right. The proportion of projects meeting all milestones I have to say defies my predictions. I thought it was mathematically almost impossible to sort of catch up and go forward, but by a very small number, we did in this most recent quarter.

Still you see that only 33 percent of projects meet every single milestone. I will say that projects have numerous milestones.

In terms of recruitment of milestones, you see a big up tick in the third quarter. I don't think this is actually due to something that we have done nearly as much as to just variation from quarter to quarter. You will see if you look at meeting recruitment milestones, we have like any other funder of research observed that our funded

projects fall behind, particularly if these are clinical trials.

The next one, I am going to go in more detail, but this is the proportion of projects that we funded that are in our judgment in the green zone. I will tell you about the different zones. The green zone is the zone we think means things are on track.

DR. KRONICK: I'm just curious. The third bar over in each of these, which represents Q-2, it looks like there was a dip in Q-2 with a recovery in Q-3, in the dark blue bar. Any reason in particular for that?

DR. SELBY: I'll check with Michele to see if anybody has ventured a hypothesis about that.

MS. ORZA: It could simply be a function of the fact that it is a slightly different set of projects each time, both in terms of new projects coming on line and also projects that are due for their six month report at that time.

DR. SELBY: I think even timing, we don't necessarily time our activities to get every phone

call made by the end of a quarter necessarily. There is a little bit of randomness from quarter to quarter. I think that is probably what Michele is saying.

A couple of things on this page. The middle, the highest set is obtained IRB approval on schedule. This is really gratifying to me that a large majority of projects have not put that forward as something they are having trouble with.

The next shows the beginnings of our work on projects that are falling behind, so you see a small number in each quarter and maybe a little bit of a rise lately in the contract modifications that are approved with regard to milestones, that is moving milestones after discussions with investigators. Contract modifications for time extensions, we are beginning to extend the time of some contracts based on discussions with the investigators.

To the right, it just shows there are a very small number of projects where we have actually had to hold funding for programmatic

reasons because they have fallen so far behind. The last one, terminated. Undoubtedly, there will be some projects that are terminated simply because they did not work out. You would expect this with 400+ projects underway. I think the next time we show this, those numbers will be larger than zero.

This is a metric that was developed in consultation with science staff to grade projects, as a way of consolidating metrics in a way we think is meaningful. If you are in the green, your project is in the green, that means your recruitment target is greater than at least 75 percent of your target, and you have hit at least 85 percent of all milestones, and the PO has indicated confidence in the project, no concerns. There, those are the ones in our view that are doing well, continued monitoring is the indication.

The yellow is the first sign things might not be going so well, your recruitment is between 50 and 75 percent, or your milestones met are between 65 and 85 percent, or the program officer has noted some concerns. There, you need to begin

increased communication with the awardee.

Orange is worse, 25 to 50 percent recruitment or 50 to 65 percent of milestones met, or serious concerns by the program officer, modifications for the milestones schedule are going to be required likely. Modifications get pursued. Red is worse than that. Significant concerns, project may be placed under review, and a draft project remediation plan is needed.

This is the way it looks. Yes?

MS. HOLE-MARSHALL: I just had a question, do you mean on the time frame that was initially agreed to?

DR. SELBY: I think “target” means at a certain date you will be at a certain point.

MS. HOLE-MARSHALL: Even if you are in green and at 75 percent, the expectation is still you will get to 100 percent.

DR. SELBY: Yes, you’re a little bit behind maybe, it could easily be rectified.

MS. HOLE-MARSHALL: Thank you.

DR. SELBY: I should just say from now on,

I think reporting to you on the proportion of projects that are in this green zone will be one of the key milestones or key milestone summaries that we will present to you on the Dashboard.

This just shows the first two quarters. This reminds me of a nice healthy salad with the predominance of green but also some red, yellow, orange veggies. You will see most of the projects are indeed in the green zone in both quarters and small numbers in yellow and even smaller numbers in orange and red.

MS. HOLE-MARSHALL: Joe, using that slide but then going back to the slide about where the projects are in terms of renegotiating and then there was zero, I think, in terminations. How long would you stay in red before you need to seriously consider removal?

DR. SELBY: I think you begin considering it as soon as you hit red, I think, but it is a very serious step to terminate a project, and it actually has some procedures/processes you have to go through, and a lot of discussion with the

institution and investigator, too. It takes a while. It takes several months, I think, really to get from seeing the red to making a termination, if the remediation plan doesn't work. I don't think we have a rule of thumb about how long.

MS. HOLE-MARSHALL: I think in addition to seeing those that are in green, I would be interested in learning more about whether we are terminating at all. I think a healthy organization has to acknowledge that some projects aren't going to be successful, and that is not necessarily a reflection even on those particular investigators. It could have been an issue of recruitment that was not known at the time. I do think we need to make sure we are able to make tough choices.

At some point I suspect we wouldn't allow folks to remain in that red without actually moving to that step. I do understand proceeding with caution.

DR. SELBY: I definitely agree that we will be showing the proportion in red and proportion terminated going forward.

CHAIRMAN NORQUIST: At NIH, they do that very similarly. You do need to have a cut off point at some point where you decide at this particular time point, we are basically going to say that's it. I don't know what that is but that is something to think about.

DR. SELBY: That's a good point. I'll take that back to the team.

DR. SIGAL: I would agree, and I agree strongly with Leah as well. Oversight and enforcement is really important in meeting expectations and having the ability if they are not to really intervene early is really important. Lots of clinical trials I see started, their stated goals never get met, and frankly there isn't a lot of ability to basically say you're not meeting goals and if you don't, there will be consequences. I think this is a very big issue in academic institutions.

When you say the green's are meeting goals, how often are we monitoring this? What is the time frame? Do you do it quarterly? When do

you basically decide on their meeting goals? What is the mechanism that we have?

DR. SELBY: My impression is quarterly. Let me check with Michele.

MS. ORZA: The formal reporting is done through a six month interim progress report, but the project officers are in much more continuous communications with the PIs, especially if they are in the yellow, orange, or red zones. Recruitment is monitored much more closely, more like monthly.

DR. SELBY: This is just a little bit of data on recruitment. Of the 190 projects that have involved recruitment, as of quarter three, 31 had not yet started recruiting, 136 are in recruitment now, and 23 have finished recruitment.

Did the recruitment initiation start on time, and the answer is for 58 percent, no, it was late. For the remainder, it was either on time or even a little bit early. Delays in finishing the protocol, the intervention protocol, and IRB delays were the two most common reasons for delay in getting recruitment started. Sites withdrawing

after randomization, and you can see the others there.

There is a milestone. There are milestones in the contract. These are contracts. There are milestones in the contract and it meant it fell short of the milestone.

DR. McNEIL: It strikes me that recruitment is the most important thing we do.

DR. SELBY: Yes.

DR. McNEIL: We are not going to get anywhere unless we have recruitment. I can imagine I could write a PCORI grant and have fairly generous milestones for myself, and I enroll the first patient four months after --

DR. SELBY: The milestones are negotiated before the contract is signed. They are not what somebody writes in the grant.

DR. McNEIL: I would love to know, and maybe Michele can do this for a subsequent meeting, tell us exactly what is “late,” by how many months, and what the percentage is for those distributions. It strikes me that the IRB delays -- those IRBs are

terrible.

DR. SELBY: Michele just reminded me that we have some information there. I can't tell you the definition of "late" but I can tell you quantitatively the length of the delays. Most of them, the real majority of them, are three months or less. These are the number of projects. Well over half of them are three months or shorter.

DR. McNEIL: It strikes me that if a protocol or project, there are five of them, are nine or more months late, why would we continue funding them? This might be a rhetorical question or maybe it's not rhetorical. Nine months is a long time. They are eating away a big chunk of funding.

MS. HUNT: I will say this based on a national trial that we are doing --

CHAIRMAN NORQUIST: Barbara, you are making a comment, but I didn't know if you had another question.

DR. McNEIL: [Inaudible.]

CHAIRMAN NORQUIST: You need your

microphone.

DR. McNEIL: I'm sorry. Why wouldn't we eliminate people, the 15, 13, 12, 10, and 9, and maybe even ask about the eight-month delays? Those seem extraordinarily long. It could have been another grant that could have been given that would have started just like that.

DR. SELBY: We will prepare this --

CHAIRMAN NORQUIST: I think we do need to know the particular situation, but I would absolutely agree. When I was NIMH, we had this as a big issue. We set a rule basically that if you didn't meet your targeted goal by recruitment within six months and we gave you like the next quarter, you were cut off basically, for the very reason we are missing an opportunity to fund other people. Ellen?

DR. SIGAL: I agree strongly. I will tell you based on a national trial that we are doing, the IRB is a huge issue, but often if you're using the central IRB, even if people will use it, the institutional review and institutional commitment

is also another issue. Even if you have it, what we are finding is different institutions may want their own review which adds two to four months.

I actually strongly agree that after six to nine months, if you don't recruit, you're gone.

CHAIRMAN NORQUIST: Bob and Debra first.

DR. BARKSDALE: I actually have a different question.

CHAIRMAN NORQUIST: Bob?

DR. ZWOLAK: I don't disagree at all with the comments made. These can be very good studies. These are good people. Sometimes they have set their recruiting goals too high. If they're not doing anything, I agree they should be cut off. I think that is a pretty aggressive terminal step that would be taken.

My question is do we have an appropriate process and counseling in between so we can avoid that. As wonderful and kind a human being Mike Lauer is, he has a whole team of people working for him that are kind of the enforcers, I think, that make sure people try to toe up to the line in the

NIH trials. Do we have that mechanism set up?

DR. SELBY: I think we actually do. I think we have very clearly written out procedures for dealing with both late projects and projects that approach the need for termination. Again, we will come back to you next time.

DR. BARKSDALE: On the previous slide, what does “restrictive enrollment criteria” mean?

DR. SELBY: I think it means somehow the investigators had settled on a set of enrollment criteria that made it very hard to find eligible patients.

DR. BARKSDALE: I guess my problem is they set the criteria, then you can’t use the criteria that you set as a reason for why you can’t enroll.

DR. SELBY: We approved them, too. I think sometimes you live and learn. The real world can surprise you once in a while.

MS. ORZA: Joe, on the ones that are severely behind, the next slide shows one, sometimes projects do catch up. Two, all the ones that are six or more months behind are in the

yellow, orange, or red zone, and they are under discussion. They are either having their milestones modified or they are getting an extension or they are being terminated. Those are all being looked at closely.

DR. SELBY: Thanks, Michele. I wanted to say this one just shows nicely that whether you got your recruitment started on time or not, had no predictability for whether you finished recruitment on time or not. There is just no association, it's a wash.

This is the last slide. Anything else? Great discussion already. We will really come back to you with details about our processes for managing awards that fall behind.

CHAIRMAN NORQUIST: Leah?

MS. HOLE-MARSHALL: Another metric that would be useful is if we are modifying, there should be a different slide for the ones that have a modified contract. If you modify the terms and then they are suddenly on time, it would be appropriate. Obviously, there was a contract

negotiation to do so and everyone felt that was an appropriate thing to do. It hides what has changed versus what has always stayed on time. Having those as a separate one would be useful.

CHAIRMAN NORQUIST: I agree.

DR. KUNTZ: One other metric just to re-update the completion date and publication date. That would be a more realistic and practical reminder to everybody, I think it would be much more of a reality check to see if this study continues at this rate, it won't be done until 2025, as opposed to just the single variable are they behind in recruitment.

CHAIRMAN NORQUIST: Okay. Thanks. We have been asked to please make sure people use their microphones and say their names, people listening on the phone are having a hard time following.

Joe, is that it?

DR. SELBY: That's it.

CHAIRMAN NORQUIST: Thanks very much. The next item on the agenda is consideration of our

annual budget. Larry Becker, who is chair of our Finance and Administration Committee, and Regina Yan, who is our Chief Operating Officer. Larry?

MR. BECKER: I just wanted to thank a whole host of people, starting with the finance team, the members of the FAC, the committees of jurisdictions for each of these elements. It just keeps getting better, and key people are focused and getting more focused on all these topics.

I think you will see as a result of the presentation Regina is going to make in a moment, a lot of work went into this. I think it is getting clearer and clearer and I think we are getting a really good handle on the inflows, the outflows, and what our future holds in terms of the finances.

While we have all identified the issue of not being able to maybe put out as many projects as we would have liked, we have a good handle on financially how to address that.

With that, Regina?

MS. YAN: Thank you, Larry. Today we are presenting to you our proposed 2016 budget for your

review and approval. First, we would like to go over the key items on the agenda today. We will review some of the key definitions of terms. We will be looking at budget development processes that we have taken, what happened before we got to this point, and then we will look at the 2016 proposed budgets. We will also look at our award commitment plan, our cash balance, as well as our 2016 staffing plan.

First, we want to go over some key terms. These terms are quite important in understanding the materials that will be presented and things we will be discussing.

One is “award commitment.” Award commitment refers to the amount of funding PCORI intends to award or the funding we have already awarded. Most of these awards are made in the form of multi-year contracts for research, infrastructure, and engagement awards, the three major components of the awards that we make.

This only refers to the funding commitment that we make. That means every time we are

bringing to you a slate of projects for you to approve, once you approve it, that is considered a commitment. The commitment is counting the entire amount that is committed at that time. Even though it is multi-year, the expenditure will take place over a number of years.

We talk about award expenses. Award expenses refers to the actual expenses incurred for the projects we fund over a number of years. When we look at a budget, the number you see is the expense. That means for all the projects that were funded, what would actually be the expenses that we would see during that fiscal year.

Once you approve the awards, we consider that commitment. Then the staff would proceed to negotiate and execute the contracts. Once the awardees start the projects and they start sending in the invoices and seeking reimbursement, that is where the expense comes in.

These are very distinctive different categories/terms we need to bear in mind.

Another one is program support. Program

support is in the budget. That refers to all the operating costs associated with science, engagement, dissemination, and contract management departments. These are the key departments that actually directly deliver a program.

Program support is important because generally with non-profits, all the costs are put into three categories. It tends to be program services, administrative expense, and fund raising. Of course, at PCORI we don't have fund raising. We have broken out program expenses or program services into award expense and program support. These are very consistent terms for non-profits.

How did we come to this point with our budget and what kind of processes did we take to prepare it. First, in 2013, the Board approved our strategic plan and also three-year priority activities, from 2013 to 2015. The priority activities simply are the major activities that we plan to implement in order for us to really meet our institutional objectives.

Early this year in February the Board

reviewed the strategic plan again and we also developed our 2016 to 2018 priority activities. Based on that, the staff drafted an operating plan for 2016 as well as the budget that goes with it. It went through internal review at the staff level, going through all the chiefs, and then over the summer we also review our draft budgets with FAC as well as all the relevant committees so you can give us feedback early on so we can incorporate all that feedback and questions into our final budgets.

Today we are bringing to you the proposed 2016 budget for your approval. Here is our proposed 2016 budget. These represent our estimates/projections of our revenue and expenditures for 2016. For revenue, we are projecting $491 million, which includes three separate streams. PCORI's revenue comes in three forms. One is appropriations, which is $120 million a year. The second is CMS transfer, and the third is PCOR fee.

As far as the PCOR fee, it is still a relatively new fee. We use the estimates from CBO,

and sometimes because it is still new, the estimates get refined and adjusted over time. For example, in 2015, in our original budget we were projecting our revenue at $462 million. At the end, we got $422 million, so a difference of $40 million.

What we do is we base on the closest estimate/information that we have, and as time goes by, we make an adjustment based on information we have.

If we look at the expenditures for award expense, 2016, $331 million, which represents 78 percent of our total budget. Program support, $53 million, which is 13 percent. Both award expense and program support we consider program expense. Administrative support is $38.9 million, which is about nine percent of our total budget.

I will go over the details a little bit comparing it to our 2015 budget as well as 2015 projected expenses. Here we are comparing our 2015 budget that the Board approved, as well as the 2016 budget we are proposing to you. One thing I do

want to note is the 2015 budget was prepared last summer, a year ago, and obviously we need to look at what we think the actual expenditures will be.

If we are looking at the 2015 budget, we had a total budget of $361 million that the Board approved, and we are proposing the 2016 budget at $423 million, which is a $61.9 million increase from budget to budget.

If you compare the two budgets, you may note that between 2015 and 2016, we are looking at a $59 million increase in award expenses, and obviously as we continue to make awards, make commitments, we will see those expenditures coming in, award expenses will increase.

We are actually asking for $7 million less this year for program support, when we are comparing 2015 and 2016 budgets. The main reason is because in 2015, when we are looking at the budget and actual expenditures, program support is one area that the actual expense is much lower than the budget. I will explain a little bit more later why.

Administrative support, increase of $9.4 million, mainly because 2015 was a year of high growth for PCORI, so we had significant staff growth in 2015, and we will be seeing those coming in in 2016, that is expected as we approved the plan for growth in 2015.

I am going to move on to talk about 2015 projection and 2016 proposed budgets. What is a projection? Basically, this is a forecast about expenditures for the year. We look at our actual expenditures through June and July. That is the time we were preparing our budget. We just closed August. We won't know about the total year end expenditures until probably November, with some preliminary, and in February, of course, the auditor will be presenting to you our actual audited financials.

We looked at our actual expenditures through July, and then we make an estimate of what our expenditures in August and September will be, and that is how we come up with the 2015 year end projection of expenses.

For the 2015 projection, we are projecting total expenses at $312 million, 80 percent in award spends, nine percent in administration, 12 percent in program support. With 2016, the proportion is more or less the same. However, total expense going from $312 million to $423 million.

Here we are looking at our projections for the total expenses for 2015 comparing to 2016. For 2015 we are projecting $312 million, which is about 13.7 percent less than our budgets, and it is expected our actual expenses will not always be exactly what we budget. I think within 15 percent is probably okay. We obviously would like to be much closer. I think moving forward as we have more historical data with our spending, it will help us be more accurate and more precise in our planning of costs.

The last couple of years have been very challenging because we have a lot of new staff, a lot of new activities. It was a little bit hard to project timing, how long things would take and how much it would cost. Progressively, we have a much

better handle on our costs.

If we look at 2015, if we compare the three categories of costs, we were pretty close when it comes to award spends and administrative support. It is the program support part, we were almost like 40 percent below our original budget. That is an area that we are trying to focus more on, examining it to help us plan better. Partly because a lot of the activities could take longer. We have a lot of new staff joining us. I do expect that moving forward progressively, we will have a better handle on those costs.

Another thing is if we look at contract management, our budget was $11 million for 2015, and actual costs, $6.2 million, mainly because a lot of the activities in contract management, which is merit review and all those things, we have done it for quite a few years, and we are able to streamline those activities. We are able to enjoy a lot of cost savings in those areas. As a result, the budget for 2016 is almost level, a very modest increase.

If you look under program support, there is an $11.5 million increase in science, program development and evaluation. One thing is because in 2015, that is the year that we have the most significant staff load, that we brought in a lot of staff to do the work that needs to be done. As a result, we anticipate the costs from that is going to show up in 2016.

We anticipate that there is a significant increase between 2015 and 2016.

A lot of that represents the additional staff we brought on and also some new activities we have to do. We talk about peer review, dissemination, all that work we must do.

Another line item that we are seeing increase is in management in general, $11.4 million increase. What drives that increase is 50 percent of that increase is in personnel, but it is not all personnel in administration because more than 60 percent of personnel are staff in the program support area. A portion of the costs is considered administrative activities, like staff meetings,

things like that, so a portion of all those staff costs get allocated to administrative support.

Twenty percent of the cost increase is in IT infrastructure. One thing is IT infrastructure is not used simply by PCORI staff. We need to support a significant IT infrastructure for all our external stakeholders, all our applicants are using our on line system to submit applications. Reviewers are using our on line system to do merit review. Annually, we have people applying to serve on our advisory panel. All that IT infrastructure needs to be maintained and supported. Again, it is not simply used by PCORI staff, but all the stakeholders who participate in PCORI activities.

If you look at the 2016 budget, 78 percent of that is in award expense, 13 percent in program support. A lot of that increase is related to a lot of new activities that we have to support, some new portfolio's we have to support, and nine percent in administrative support in 2015 and also 2016.

What is nine percent? Is it good or bad?

We have done some benchmarking. Of course, no two organizations are exactly the same. We do the best to look at several similar organizations. The benchmark, 11 percent. I think we compare quite favorably at nine percent. Of course, our objective is to be able to do the most and most efficiently. We will continue to monitor our administrative support expenses.

I know the Board is not only interested in 2015 and 2016, you are also interested in seeing the out years, over time, what our planning looks like. Here we are looking at revenue and expense. The green bar shows our revenue. We know our revenue more or less except for the exact amount of the PCOR fee.

We know we have revenue through 2019. The green bar stops at 2019 because that is the period of the revenue that we know at this moment. In 2013, we presented to the Board a couple options about how we plan to spend the revenue we know.

The Board made two decisions. Number one is we want to fund as much research as early as

possible, so we can get results as soon as possible. Second, we also want to make funding available all the way through 2019.

Based on those two guidelines, we planned out our revenue and expenditures. You see the revenue stops in 2019 because that is the period that we know what our revenue will be, and then when we make a commitment all the way through 2019, we will see the award expenditures being spent over time. Assuming we make a three year award in 2019, the project would take place in 2020, 2021, and 2022, and finish all the project activities. In 2023, we have an one year period to do peer review and dissemination and then we close everything out in 2024. This is our projection through 2024, looking at our revenue and expenditures.

Of course, the core of our program and activity is funding research with funding commitments. This is our funding commitment through 2019. We plan to make funding awards in the amount of $2.5 billion, 84 percent will be in research, 11 percent in infrastructure, PCORnet.

Any demonstration project, research project, that is done within PCORnet goes into the research column because that is considered research. Five percent in engagement and dissemination.

Based on that plan, at the end of 2016, we expect to have awarded $1.8 billion. That is 71 percent of the total $2.5 billion, what we plan to commit.

I think this plan probably meets our objective of funding as much research as we can early on.

This shows the composition of our commitments in 2016 for research infrastructure. Engagement is a very small portion. We are not including that here. For 2015, 50 percent is in targeted and pragmatic. In 2016, those two categories go up to 62 percent.

CHAIRMAN NORQUIST: I am sorry to push you, we need to have some time for discussion.

MS. YAN: I can go quickly. This shows our accumulative award commitment and award expenses. Since we make commitments early on and

it gets spent over time, you see in 2016, there is a big gap between commitments and expenses, which you will see in the next two slides.

For example, at the end of 2015, our cash balance will be $737 million. We have a spending obligation of $800 million. Of course, that would not create a cash flow problem for us because the outstanding obligation is paid out through a number of years. We are not sitting on all the money, it is all obligated.

At the end of 2016, our cash balance would be $805 million, and we would have over $1 billion in outstanding obligations.

The last one is our staffing plan. We have 24 positions in 2015. We are proposing another 33 positions, many to handle new activities in peer review and dissemination. You can see that 75 percent of the new positions is in science, engagement, and contract management. At the end of 2016, we will be looking at 257 positions.

That is the end of the presentation.

CHAIRMAN NORQUIST: Larry, did you want to

say anything? Then I will go to Harlan.

MR. BECKER: He can go ahead.

CHAIRMAN NORQUIST: Harlan?

DR. KRUMHOLZ: Thank you very much, Regina. We appreciate all your hard work on this. We know it's a lot. To Larry, the committee, and everyone else that has been involved, because this is not easy.

I just have a couple of quick questions. One is just personal interest. When we are done, what will have been the amount of money that will have been allocated to us in total? Do you have a projection on that?

MS. YAN: $3.3 billion.

CHAIRMAN NORQUIST: That's an estimate, remember, even next year, it's a projection, we don't know exactly how much we will get.

DR. KRUMHOLZ: I was just wondering. I have generally been seeing $2.5, I didn't realize the projection is $3.3. What percentage of that, given what you are seeing here, will have gone to research at the end?

MS. YAN: It is $2.5 billion of funding commitment, that is the award amount we are looking at.

DR. KRUMHOLZ: $2.5 of $3.3?

MS. YAN: Correct. $800 million goes into program support, that means people who actually oversee all these awards, contract management, and administrative support.

DR. KRUMHOLZ: That $2.5, that includes PCORnet. I would consider that actually research awards. That $2.5 includes PCORnet?

MS. YAN: The $2.5 includes PCORnet, but not including PCORnet engagement, it is $2.1.

UNIDENTIFIED: The $2.5 is all hard research, not administrative or other contracts or other things?

MS. YAN: It is all to the awardees, what you approve.

DR. KRUMHOLZ: The $800 million is for the other.

MS. YAN: Program support, administrative.

DR. KRUMHOLZ: The $2.5 is going to

research.

MS. YAN: The $2.5 includes research, infrastructure, and engagement, and $2.1 is purely research.

DR. KRUMHOLZ: Just curiosity, our money that sits in the bank, is that put anywhere? What happens to that?

MS. YAN: The majority of our money is in the PCOR Trust Fund, it sits in the treasury. We only draw whatever we need. We do have money we kept in the operating bank account, but most of it is in the PCOR Trust Fund.

DR. KRUMHOLZ: I do want to make just one general comment for the public, how hard it is to benchmark the percentage that goes to direct research because we started from zero. Benchmarking against an established organization that is in a steady state versus one that is building up from nothing, I don't know what the right benchmark is, but I just want to make a public comment that is a difficult thing to do given our history and what we have tried to do.

In that spirit, one thing, and this is just for the whole group to think about, I'm just thinking about how much of what we have done can be repurposed or made available for the public good when we are done.

For example, if we spent a lot of money developing software programs for people to submit grants, is that open source, can we just give that away? There is some possibility and I think we are all hopeful that we can continue, but even if we can continue, there may be ways for us to make available things that we have invested in so that no matter what, some marginal costs that someone might pay, they can take advantage of the kind of things we have developed, if someone wants to start a new foundation.

These are the kinds of things that we can find additional purposes for the policies and procedures, and all that work to build an organization can be available to someone else who might want to do this, anywhere in the world.

It is just an idea for us to be thinking

about, there is stuff that we have done, we felt the same way about research, how can we have reasonable research networks. I think when we are going into an investment in an organization, we should think about reusable, anything that is reusable in what we have created, we ought to be seeking ways to ensure other people have access to it.

Thank you, Regina.

CHAIRMAN NORQUIST: As you point out, it could be somebody starting a foundation today; yes. That is a good point.

DR. JESSE: I'm sorry if I missed this. In Joe's Dashboard, we were under allocating research money, and yet we are sitting against an allocated budget. What happens to the money that doesn't get spent in a particular budget year that was otherwise allocated to go out?

MS. YAN: Because we have our commitment plan all the way through 2019, every year we make some adjustments. If we have in one particular year, when it comes to commitments, that we are not

committing up to the limit we thought we would, then it goes to the following year. Sometimes some of those are already in the works but maybe does not make it to the fiscal year.

If you are talking about program support, say under spending --

CHAIRMAN NORQUIST: Wait Regina, I think his point is we propose to spend a certain amount and then we don't. I think what happens is we recommit that, like some of these new RFAs we want to do, program announcements, or something like that.

DR. SELBY: We aim, since 2013, we have aimed to commit more than we have taken in. We have more obligations than we have revenue through the end of 2015. We actually fell short. We actually intended to commit more and to have a greater discrepancy at this point, so the shortfall is in commitments. What actually happens to the money, it stays in the Trust Fund until the researchers we have committed to invoice us.

We're not like a Federal institution which

has to spend its money by September 30.

DR. JESSE: If we don't commit what we allocated, say we don't fund as many grants as we expected to fund, which was my sense of what was happening there, that just is more available into the future.

DR. SELBY: Yes. The initial projection that we drew in 2013 had us committing less than $90 million in 2019, just really getting down there. I think now it has flattened a bit. We are still committing in advance of our revenues, but it is not as extreme as we thought. There is an up side and down side to that.

DR. KRONICK: Joe, just an important caveat to Bob's question, that is all true up until 2019, when the Trust Fund gets turned off. That is why I think it is very important that we follow a trajectory that allows us to make the total number of commitments by that time.

MS. HUNT: I would just like to suggest that we really be sure, now that we are moving along and we have results that are starting to come

out of our research, and that's going to continue, we need to be sure we are appropriately and strongly staffed up for engagement and implementation and dissemination.

I don't see a lot of that in here. I see a couple of additional positions being added. I think that is really important, that we give the public the understanding that we are going to be moving to disseminate what we are coming out with as results. As you mature as a research organization, we have to be focused more on that.

MS. YAN: So far we have not had a lot of dissemination expenses yet, we are starting in 2016. As you mentioned, we have new positions for that. It is our plan that in 2017 to show those expenses to you.

CHAIRMAN NORQUIST: Bob?

DR. ZWOLAK: Following on Gail's comment, I know we are obligated by the law to do peer review and release our results. In the last six months, there was an estimate that it would take six to nine months for our results to make their

way through the peer review process. Is that a limitation based on the number of people you are hiring or is that a real limitation, is it a limitation based on number of people you are hiring or is it a limitation purely due to the complexity of the process?

DR. SELBY: Complexity of the process entirely. Think about when you submit an article to a journal and it takes back and forth between you and the reviewers, sometimes a couple of times. There may actually be more negotiation when you are negotiating about the final report that we are going to put on our website, sometimes it is incumbent on the investigators to actually make changes and get back to us, we take a look at it again. It takes a bit of time.

We also give them sort of a period of time at the beginning to finalize the report, the draft report, before they submit it to us. I think that is just a realistic estimate of the time for the peer review process to take place.

MS. YAN: However, peer review does not

prevent the investigators from publishing their findings somewhere.

CHAIRMAN NORQUIST: Any other comments?

[No response.]

CHAIRMAN NORQUIST: I need a motion to approve the budget.

UNIDENTIFIED: So move.

UNIDENTIFIED: Second.

CHAIRMAN NORQUIST: Any further discussion?

[No response.]

CHAIRMAN NORQUIST: The way we will vote is I just need you to raise your hand in the room if you are in favor of the budget.

[Show of hands.]

CHAIRMAN NORQUIST: On the phone.

DR. DOUMA: Aye.

CHAIRMAN NORQUIST: Freda?

DR. LEWIS-HALL: Aye.

CHAIRMAN NORQUIST: Harlan Weisman, I do not think is coming on until after lunch. Anybody opposed in the room? Anybody abstaining?

[No response.]

CHAIRMAN NORQUIST: Thanks. Thanks, Regina and Larry, and to the committee also, who did a good job.

MS. HOLE-MARSHALL: Gray, can you just announce for people on the phone that it passed?

CHAIRMAN NORQUIST: It passed, for those of you on the phone. Thank you, Leah. Unanimously, I should point out. The next item is slate of spring 2015 broad awards, broad announcements. This will be led by Christine Goetz, chair of our Selection Committee, and Bryan Luce, Chief Science Officer. Christine, do you want to start?

MS. GOERTZ: Thank you. We are excited to present the slate of broad announcements. We actually have three different slates that we will be asking for your approval on today.

The first is the broad, and this afternoon we will be presenting our initial slate for Hepatitis C, as well as our slate for pragmatic trials.

Just a reminder, with the broad slates, we generally present the information, the titles of the applications so you can get a sense of exactly what types of research we are funding, and Bryan will also provide some summary data on location and dollar amounts, et cetera.

Bryan?

DR. LUCE: Thank you very much, Christine. As Joe said earlier this morning, I want to just say a very few words, I'd like to take this opportunity to express my deep appreciation to serve as your chief science officer, and to serve you, Joe, in particular.

It has been a true honor not only to serve the Board, actually I think of it as the country, and to Joe, but also to work with just an amazingly dedicated and wonderful professional staff that we have all put together.

That is it, I just wanted to let you know that I have had the project officers.

DR. McNEIL: Can we ask a question now or do you want us to wait?

DR. LUCE: I think you need to wait because I'm not going to be prepared to talk at any depth on any particular one. The project officers are not necessarily even here.

CHAIRMAN NORQUIST: Part of the issue here is that when we are voting, now Mary is going to stand up here, because we get into this issue about if you get into the details of the project, then we expose -- I think if you want to talk about the topic in general, that's fine.

DR. McNEIL: I did. The question I had, and I think I sent this in an e-mail to somebody, I thought there was a study on active surveillance versus care for DCIS that came out quite recently. It did come out quite recently; I know that for a fact.

CHAIRMAN NORQUIST: Christine, you're on the Selection Committee.

MS. GOERTZ: We actually did discuss that study. I think the general consensus was it wasn't completely definitive and there was more opportunity for knowledge to be gained through this

particular study. We did bring up your concern when we talked about this and decided the study would make an important contribution.

CHAIRMAN NORQUIST: Basically, in answer, you didn't feel the study was definitive, that there was more work that could be done, and that is why you are proposing it.

DR. McNEIL: Just as a P.S., I think when we announce this; I think it would be really critical to add that to the announcement. On the fact of it, it looks like we are being redundant.

CHAIRMAN NORQUIST: Okay. Basically, we are announcing it now because we are doing this in public.

DR. LUCE: This next slide indicates three recommended projects by the Communication and Dissemination Research Program. Here we have five recommended projects from the Improving Healthcare Systems Program. Here is the slate from Improving Methods for Conducting PCOR.

In summary, here is actually what we are recommending. That first column is what was

announced in terms of funds available for this cycle, totaling $88 million. We are proposing a total budget of $54 million for committing in this slate. The average project budget is $2.251 million. That is consistent with what we have been doing all along in terms of funding, a little bit less than the total we absolutely had available. We announced that we are interested in funding up to this amount of money. There is one program that was a little bit higher than its allocated amount.

CHAIRMAN NORQUIST: Are you finished, Bryan?

DR. LUCE: I am.

CHAIRMAN NORQUIST: Okay. Christine, did you want to say anything else?

MS. GOERTZ: No, I don't have anything to add.

CHAIRMAN NORQUIST: We will have some discussion now. Barbara?

DR. McNEIL: I thought it was a nice presentation, Bryan, thank you. I have one question, the 38 percent of the grants that were

awarded as having been resubmissions, do we know how that compares with various institutes at the NIH?

The second question is do we know on the revision, the second submission, whether the revisions -- how substantive they had to be. I know at one meeting we talked about the fact that people were uncomfortable with the PCORI format, whether some of the revisions had to do with getting more into the PCORI format.

A, is 38 percent consistent across the board, and B, how substantive were the revisions that were required?

DR. LUCE: I don't have it on the tip of my tongue what the NIH resubmission rate is. Others may.

CHAIRMAN NORQUIST: Was that a percentage of the funded grants?

DR. LUCE: Yes.

CHAIRMAN NORQUIST: It usually is much higher for resubmissions at NIH. I don't know the exact number and it will vary by institute. It's

too bad Francis is not here. Just from my experience having worked there, a high number of those that were funded, and of course, it has gotten a little tougher now because you only get so many times to resubmit now at NIH. It used to be unlimited. We have unlimited.

MS. GOERTZ: My sense is it is similar, and I just asked Rick where it was at AHRQ, and he said it is similar to what we are finding as well.

DR. LUCE: Actually for this cycle, we were fairly pleased with the rate.

CHAIRMAN NORQUIST: I know at NIH, it will vary by the review group because some are very tough, it's like a paper, you never get it accepted the first time, you always have to come back and do something.

Any other questions at this point?

[No response.]

CHAIRMAN NORQUIST: One of the issues that has come up, which we will discuss more, is about the Board's role and what we are doing here, and I think what we are doing is we are approving the

funding. We are using our fiduciary responsibility here to approve the funding and the general topic areas. That is our role here at this point, and the process where the Selection Committee had the more in depth role.

To be honest, Bryan, the problem with the titles sometimes, not so obvious, I tried to pick out, there was a fair percentage of mental health, but I couldn't pull it out. I saw one grant that was clearly mental health. I couldn't figure out where that other mental health was in these topics.

CHAIRMAN NORQUIST: I need a motion to approve this broad slate.

UNIDENTIFIED: So moved.

UNIDENTIFIED: Second.

CHAIRMAN NORQUIST: We are going to vote again like we did before, if you will raise your hand if you are in favor of the slate.

[Show of hands.]

CHAIRMAN NORQUIST: I will ask the people on the phone. Allen?

DR. DOUMA: Aye.

CHAIRMAN NORQUIST: Freda?

DR. LEWIS-HALL: Aye.

CHAIRMAN NORQUIST: Harlan, are you on? Weisman.

[No response.]

CHAIRMAN NORQUIST: Anyone opposed in the room? Anyone abstaining?

[No response.]

CHAIRMAN NORQUIST: That passes, for those on the phone, unanimously.

DR. FERNANDEZ: Could you please let the record show that I'm recusing myself.

CHAIRMAN NORQUIST: You're recusing yourself. You are recusing yourself, too?

DR. KRUMHOLZ: I'm recusing myself.

DR. FERNANDEZ: As members of the SOC Committee, we are un-blinded as to some of the investigators involved, and I am consequently recusing myself.

CHAIRMAN NORQUIST: All of the people on the SOC need to be recused?

MS. GOERTZ: She means the Selection

Committee.

CHAIRMAN NORQUIST: Who else is on the Selection Committee?

MS. GOERTZ: We have never done that.

UNIDENTIFIED: Gray, it is not all the members of the Selection Committee.

DR. McNEIL: Alicia identified one because she had been un-blinded and she had a conflict.

CHAIRMAN NORQUIST: I see. Harlan was adding it in. Okay. We have settled that issue now. Thanks. Anything else, Bryan?

DR. LUCE: No. Thank you.

CHAIRMAN NORQUIST: We are five minutes early for lunch. At this point for those of you on the phone, we will be back at 1:15 Eastern Daylight Time after we take a break for lunch. Thanks.

[Whereupon, at 12:10 p.m., a luncheon recess was taken.]

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

[1:17 p.m.]

CHAIRMAN NORQUIST: I want to welcome everyone back. We are now going to move to our next agenda item, which is the first of what will be a regular feature of our Board meetings, something we have been asked to do for quite some time, our Stakeholder Perspectives Panel.

Today's panel features senior officials of health plans, and the Board looks forward to engaging in the future with a wide variety of stakeholders. You guys are the first, and we are very pleased that you could join us.

Our vice chair of the Board, Kerry Barnett, will be moderating the panel. Kerry, if you want to introduce the panelists and start it, we will let you run this session.

MR. BARNETT: I will do that. Joe, did you want to say anything first?

DR. SELBY: No. I think between Gray and you, you will introduce these fellows appropriately.

MR. BARNETT: Okay. First, thanks to both of you for being with us today and for helping to launch what will soon we hope be a tradition. My job as moderator, I think, is probably the easiest assignment I could have.

I am just going to very briefly introduce each of you, and then we will turn you loose with some prepared comments. Then we will open it up for questions and comments from the group. Does that sound okay?

On my far right is Dr. Sam Nussbaum, who is Executive Vice President for Clinical Health Policy and Chief Medical Officer at Anthem. He is responsible for the company's public health policy programs. He is also responsible for clinical strategy, medical and pharmacy policy, and clinical quality programs. He is also responsible for HealthCore, Anthem's clinical outcomes research sub.

Prior to Anthem, he served as Executive Vice President for Medical Affairs at BJC Health Care, and President of its medical group. He also

serves as Professor of Clinical Medicine at Washington University School of Medicine.

Sam, thank you very much for being with us.

I will also introduce Dr. Lewis Sandy, immediately to my right. He is Executive Vice President at UnitedHealth Group, been there since 2003; right? His focus is primarily on clinical innovation, physician collaboration, and reforms related to provider payment and the delivery of health care.

He is also a principal at the UnitedHealth Center for Health Reform and Modernization. He has also served as Chief Medical Officer at UnitedHealthcare. Prior to that, served as Executive Vice President at Robert Wood Johnson.

Thank you to both of you for being with us today. Sam, we will start with you, if that is all right.

DR. NUSSBAUM: Thank you, Kerry. Thank you, Gray. Thank you, Joe. It's really a pleasure to be here at your inaugural forum with key

stakeholders.

I also think it is really important that we talk about a path forward because many of us have been strong supporters of patient-centered outcomes research and the work that you have done, and really see this as an enterprise that needs to build on its success.

I also want to thank this Board of Governors because it is interesting and you acknowledged this over lunch, that so many of you have been with PCORI since its inception, and like the birthing process, made the adolescence of seeing an organization through some challenging times, determining its sort of strategy. This may be a really good opportunity at the five year point of the initial decade to look at what changes can be made to make this wonderfully sustainable.

At Anthem, we have been major supporters of effectiveness research and outcomes research. In fact, as we talked about and were reminded, the original Institute of Medicine's call for effectiveness research was some work that Barbara

McNeil led. Even with the Blue Cross/Blue Shield Association, we were out there saying we would welcome the funding of such an organization.

We also within our own company have our own outcomes research subsidiary, HealthCore. It is sort of like the opening of A Tale of Two Cities and Dickens. It is truly the best of times and worse of times in health care. The best of times because of the breathtaking science that is taking place and discoveries. Yet, in many ways the worse of times, the 30 to 40 percent of what we do, which is either unproven or inefficiently delivered care, and that cost is crowding out other necessary investments for our nation, in education, housing, wage growth for companies.

In many ways, PCORI is a true jewel of the ACA, and I think as Secretary Burwell has announced recently and the private payers have joined forces, we are all committed to more value based care and value based payments.

How do you get there? One way of getting there is to really know that you are going to play

a key role in guiding the nation to proven intervention, determining what works and what works best.

There are several ideas that I'd like to develop with you or share with you today. I believe they will accelerate PCORI's success and build on its strong foundation. They are about stakeholder versus researcher-generated models of research. They are about prioritization. I know you have spent a lot of time on that, and particularly prioritization of new technologies.

They are about collaboration, and some very specific paths to engage constituencies because I think most of all, every organization wants strong allies in the path forward, and people who not only are allies but truly understand the mission of the organization and what it has achieved.

A number of the comments that I'm going to make now, I believe you have heard before, and you are on a path to change, and the model is changing. For example, when we look at this concept of

researcher generated versus stakeholder generated, that agenda has evolved and I think needs to continue to evolve, not only on funding notices covering broad topics, but really asking very, very specific research questions.

I am delighted personally to see you have done more of that, and I know you are crossing that threshold of researcher initiated versus stakeholder and PCORI driven.

At the same time this is occurring, I think there is a new strategic direction with tempo. It is occurring at FDA. It is occurring around the nation. That is an increasing focus on pragmatic clinical trials.

In fact, one of the interesting reports, while it is to the FDA or about the FDA, is the Bipartisan Policy Council has recently issued a report that says we can accelerate and improve the medical product development process as well as generation of more relevant evidence with those capabilities surrounding pragmatic research.

How could and should research be

prioritized? Again, it's an area where recognizing the delicate balance. There is an overarching statement that I think is important here. I think we should know answers before patterns of clinical practice are engrained within physicians and other health professionals. That is an opportunity.

Specifically, whether it is proton beam treatment or Hepatitis C or other specialty pharmacy areas, an area of absolutely increased focus for this nation, whether it is molecular diagnostics and targeted therapies, spinal surgery, or optimal coordinated care models, value based models. That is really work that is at its inception, and the closer the research agenda can take that on, I think the greater relevance and meaning in the change of care in this country.

PCORnet offers just extraordinary opportunities to collaborate. In fact, today, if we think about one model that has worked, I believe the FDA Sentinel system and PCORnet, they are highly complimentary, across networks of data partners, and is containing today information from

tens of millions of individuals.

With these data partners and this data, it could be even more intimately linked with bi-directional flow of information. Sentinel's drug surveillance capabilities could be improved, and PCORnet's conduct of patient-centered comparative effectiveness could be enhanced. I know it is a direction many of your colleagues have also embraced, and I know, Joe, you have been personally engaged in this. Again, that is a huge opportunity.

When you think about the clinical data research network and the patient powered research networks, these are absolutely strong conceptual models. The health plan data, I think, in many ways could even make them more effective.

I think there is consideration that some health plans believe that today it is provide us data, which of course, we want to do, but I think it is going to be in the future provide us data and be our research partner. I think this is where this is going.

Let me talk a moment about convening specific stakeholder groups. It is clear that extraordinary capability and infrastructure has been built, they are broadly constituted stakeholder committees, as the Board is.

I think it is important perhaps to focus and convene additional groups that may represent either health plans, providers, or even consumers. Well, you say Sam, why would you want to do that when you could have all the stakeholders represented. I think in this way, a more formalized process, these groups cannot only identify opportunities, but can strongly become your advocates. I will talk in a few moments about how this could be achieved even in terms of the research agenda.

What I think is important again is PCORI has established key priorities in domains that we know are worthy of investigation, the domain of just improving methodologies is going to be a foundation for later work. Like any scaffolding and any foundation that you take many years to dig,

and we all know that building the arises very quickly, all that great work will build for the future.

How do you build on this? I think we have talked a little bit about prioritization. As I close these comments, I think it is important to maybe take some topic areas that would engage broad stakeholders.

There is a recent report in Health Affairs you may have seen that talked about coverage variation amongst the payers and CMS. It turns out there is about a 50 percent divergence. Providers have said why should that be. In fact, the nation should say why should that be. That's an opportunity. There are ways of trying to find those areas where there is the most variation and understand them.

It would be interesting and you have probably done this to look back at those, remember the 100 initial studies, priorities, that were determined by the Institute of Medicine, and see how many of those actually were taken on, and

whether they are meaningful today. I think one of the high priorities was for cardiac arrhythmia, atrial fibrillation was the best approach.

That is very specific, but the concept is if you were to convene these stakeholder groups, to patients, to providers, to insurers, could a small percent of the research agenda be focused on their ideas.

In many ways, I think that type of alignment around issues, such as treatment of prostate cancer -- I know, Barbara, earlier you mentioned ductal carcinoma in situ -- autism, spectrum disorders, refractory depression, C-section. These are huge issues and areas that I know will be looked at and increasingly, I think, will be a focus of all the groups coming together as well as separately.

Just to close, I think while my comments are certainly not about data governance, PCORI and the way you use data can actually lead the way for the nation, maybe globally, on how to use big data. Working together with health plans on data

governance, working again through PCORnet and organizations that hold complimentary data, as I mentioned, across diverse networks and partners, could really be extremely important, and I believe employers will be allies. They own a lot of the self funded data. Medicaid owns data. You own data through a coordinating center, and health plans' own data.

I believe to close that the type of engagement that you have with our industry will contribute meaningfully to the development of a system that will be what you all want and what we all want, which is a broad national resource for comparative effectiveness research.

Thank you.

DR. SANDY: Thanks. I appreciate Kerry, Gray, and Joe, as Sam mentioned, the opportunity to be here. I think it says something about PCORI and the culture -- I'll make a comment on that in a few minutes -- that you invited us to hear an open and honest perspective from a payer point of view.

Before I start, I want to just make a

couple of disclaimers. First, I thought I'd comment as an individual, even though my work is informed by my time at UnitedHealth Group, which includes United Healthcare, covering about 50 million Americans and Optum, our health services company, that serves probably 80 million people, but also is involved with all stakeholders in health care and very heavily involved in research, data and analytics, part of the Sentinel network, as Sam mentioned, but I also have spent, as Kerry mentioned in the intro, 12 years at the Robert Wood Johnson Foundation before I joined United.

I realized I have kind of been in your shoes as a Board, trying to figure out how do we know whether our program of funding and strategy makes sense, and how do we know it is having an impact. I thought I'd give some comments about that as well.

The other thing is I've organized my remarks into three areas about sort of my assessment of patient-centered outcomes research as a priority, PCORI itself, what I think is sort of

my interim assessment from a personal point of view, and then some suggestions for improvement and opportunities that I see.

In doing so, I realize I'm kind of an amateur evaluator, and this is the other caveat I wanted to make. I'm pretty familiar with PCORI but I'm not encyclopedic in my knowledge, and the comments that I make could be misinformed or wildly off. Take it with a grain of salt.

PCOR, PCORI, and suggestions for improvement. Sam said it very well. In terms of the field of patient-centered outcomes research, this is absolutely essential for all stakeholders, and it is sorely needed. It is needed in two dimensions at least, and I think PCORI is optimally positioned, and I think why PCORI was launched, we need good comparative effectiveness research to inform all stakeholders, but the other thing that is critically needed is to incorporate and have a method for incorporating patient perspectives into that process at all points along the continuum. Both of those are seriously lacking in the U.S.

health care system and even worldwide.

I just think PCORI or sort of the rationale for PCORI is absolutely sound, and I think is absolutely essential. I personally want PCORI to thrive.

Coming to PCORI itself, let me give you kind of what I think has been good and what are some opportunities for improvement. My take is PCORI at this stage, you have really built the field of patient-centered outcomes research, and not by yourselves, but in collaboration with a methodology of being very open and inclusive, and unlike many other efforts that I've seen previously, often times there is a lot of lip service to the patient, so you say yeah, we're going to be patient oriented, and then we're going to go off and do whatever it is that we were going to do anyway.

That is not PCORI. Your methodology and your methods of including patients, patient perspectives, patient groups, you are walking the walk, not just talking the talk. I think that

comes through.

Related to that is you have identified the need for more rigor and more robust processes to incorporate that into research methodology from question formulation, the research methods, to engagement throughout the research process, and then including dissemination.

I think that is really powerful, really important. I'm not going to focus on the particulars of your programs. Sam had some really good suggestions. I also want to commend you for your specific focus on disparities. If you look at all the IOM mains, I think we are making progress. The least progress I think we are making is on disparities, health equity. I really appreciate that you are focused on that.

The other thing that is good about PCORI, you have attracted a lot of talent, a lot of talent in your organization, in PCORI, among the leadership, among the staff, and you have attracted this sort of network of really talented people. I know a lot of people that are involved in PCORI.

You have really good people.

The culture of openness, the culture of accessibility. The PCORI staff, I see Joe, he always says hi, we see you everywhere. I say well, I always see you everywhere, by definition, you're out there. You're out there talking about what you are doing, and you are very open and accessible. You're not in any kind of defensive crouch, which you could be in, but you're not. I think that is really commendable.

On the program, you have really started some very promising approaches. I would highlight PCORnet, as Sam did, and the patient powered research network, coming to my comments about sort of methods for incorporating patients. I think that is a really innovative idea. It's obviously early, but there is a lot of potential power there.

That's my kind of good news.

UNIDENTIFIED: Did you want to stop there?

[Laughter.]

DR. SANDY: Let me give some formative feedback, shall we say. I thought PCORI got off to

a slow start, and frankly you were in a start-up, so there is a certain amount of that that makes sense. Even saying that, I think PCORI got off to a slow start, and it wasn't much of a focus that I could tell around kind of an early win, let's put our nickel down in something to say oh, I kind of get what they are doing.

Related to that is although you laid out priorities, those priorities are very general. I know, for example, the GAO reports, some of them cited some people thought the priorities were not all that prioritized. I would share that point of view. That may be changing, which is good.

Again, we represent payers, but you have to remember, we are not payers by ourselves. We are agents or purchasers, public and private. I don't see there have been a lot of deliverables for the purchasers and payers at this time, to Sam's comments and good suggestions on how to do that.

I think generally there is pretty low visibility among PCORI, and I'll have some suggestions around that. Sometimes issues are sort

of the flip side of the strength, focus on rigor. Some of your methods and some of your approaches in my view are too academic for the applied way that this information can be most useful on behalf of patients.

I think you have in many ways emulated the NIH model, and Francis is here. The difference is I don't think Francis needs to go and justify the existence of the NIH. Maybe we can about that. I don't get that sense that people call that question very often. It's a little different with PCORI and some of your sister agencies. I think that's an issue.

The other one thinking about how to apply this investment in patient oriented research, both Sam and I spend a lot of energy on payment and delivery reform, there is a generalized lack of infrastructure, or a scalable repeatable infrastructure, for collecting data on patients. That is a real issue in the entire field, that's not PCORI's issue by itself.

Since you emphasize and represent a

patient perspective, I think you need to work more on figuring out, we have good ways, they can always be improved, good ways to measure quality, good ways to measure costs and efficiencies. These can be improved. We don't have the same infrastructure on patient outcome, and maybe PCORnet and the research networks can do that.

In closing, that is sort of my amateur assessment of strengths and opportunities for improvement. My suggestions, I think the first one is you need to create what our sales people would call a sales sheet for PCORI. I could not find it. I don't see anywhere kind of an one pager on what is PCOR and PCORI, what are you doing, how is it helping the American people or the health care system, and why should you, the reader, care. That's what our sales people call a sales sheet. You need that. Maybe I couldn't find it.

Some of the things that I did see are kind of jargony, and I think you need to do some work on de-jargonizing some of what you are doing. I think one of the things that would be helpful in

addressing something Sam mentioned and the stakeholder issue is the idea of a rapid response capability.

I know a number of health technology organizations around the world have kind of a quick way to respond to queries about what do we know about an area. PCORI could do that, do it directly, support it through grants or contracts. That would kind of help create a discipline actually. You're not going to answer every question in a short period of time, of course, but you can highlight what it is that we know and what it is we need to know in an area. I think that would be useful for you to do.

I think, coming back to my comment, you need to have some useful deliverables for your patrons. It's different. I was at the Robert Wood Johnson Foundation that had an endowment and didn't have to secure ongoing financing, but you do, with your time limited funding stream.

It's really important, and Sam said the same thing, to start to work now to showcase the

value of what PCORI is doing and the utility of it, sales sheet, other ways to do it, and work now particularly, for example, on the sustainability of PCORnet and the patient powered research networks.

Those are my suggestions. I realize a lot of success in life is basically luck and the rest is timing. The clock is ticking for PCORI, and all of us want to make sure that this capability continues to advance on behalf of the people we serve, on behalf of the patients we take care of, on behalf of the U.S. health care system, so I hope this feedback is useful, and both Sam and I look forward to your comments.

MR. BARNETT: Thank you very much. We appreciate your candor, we honestly do. Let me start by asking the first question and then we will see what comments and questions others have.

PCORI, as I'm sure you know, under statute is prohibited from funding research that focuses on cost. Payers live, as we all know and understand, in a very cost conscious world, as do the purchasers you referred to, that you act as a proxy

for.

Does that suggest sort of a fundamental non-alignment between the carriers and what PCORI is all about or is that something that can be bridged?

DR. NUSSBAUM: It's an important question and certainly one we have thought through in our organization. Even though you can't directly look at cost, what you can look at is the outcomes, and that is how we basically begin any assessment.

For example, if we are looking at -- I know we are going to hear about this later -- if we are looking at what's the most effective treatment for Hepatitis C, we want to know from a patient perspective what drugs are tolerated best, what the success rates are. We can then manage through many of the aspects of cost in terms of value of the drugs, how we negotiate those contracts. That is a very, very specific example.

One of the things we are also knowledgeable of, if you look at the IOM report of a year and a half ago on better care at lower cost,

it was really about inefficient care, waste, performing medical services that don't add value. That is where PCORI can be most effective and because of the partnership, and Lew has emphasized this, through PCORnet, we can work together to look at the real world pragmatic activities that are taking place.

Even though you may be precluded by statute, the information that you can gain will be incredibly valuable to those of us that do balance value, that do have to make those considerations.

The one thing I assure everyone here, because it is really important, for health plans, if there is a superior treatment, albeit one that may cost a great deal, we will opt for that superior treatment. It's only when you don't know whether there is a superior treatment, and it's everything appears to be the same that we are looking to find the most cost effective way of proceeding.

DR. SANDY: It's a great question. In the payer world, I think there's a spectrum. There are

some people that say you know, what is really important is to have a group opine about cost effectiveness and cost/benefit analysis, but my own personal opinion is a little different, which is I think the most critical questions are around clinical effectiveness, clinical efficacy. If those questions are answered in a comparative way, others can pick up and kind of do subsequent analysis looking at value for money.

I don't consider the way PCORI is structured a show stopper by any means.

MR. BARNETT: Barbara?

DR. McNEIL: Those are great remarks, Sam and Lew. I have a question. Both of you mentioned PCORnet several times. We have talked a lot about that here. I believe, Joe, correct me if I'm wrong, there are two pilot studies going on, one on aspirin and one on bariatric surgery for kids. The question I have for you, since you both mentioned this, A, are you dying to know the answers to those questions, and B, what kinds of questions, if you each could name two clinical questions that would

just be ideally suited to measurement or a study by PCORnet.

It is a big investment on our part, and even though you say it, I don't think we have come to real grips about what those could be. I'd love to hear your thoughts and really specifically, if you could.

DR. SANDY: I hesitate, Barbara, to give an answer off the top of my head. I'm kind of on research priorities. I'd have to think some more.

I'll give you an illustrative example from what you are already funding, both of which are kind of important questions. For example, the aspirin question is an important clinical question, but I don't think this is something plans are worrying about at night. What do plans worry about at night? They are the kind of things Sam has mentioned around typically therapies, that we think there is a great deal of variation in what is done. Evidence at least as best we can tell where that variation does not seem clinically appropriate and frankly isn't benefitting the patient, a lot of

care that is being delivered really isn't benefitting the patient.

The other thing to your question is understanding outside of traditional clinical trials and carefully selected populations, health plans and payers have to make policy that affect unselected populations of patients, so the kind of conundrums we grapple with have to do with which subgroup of patients benefit the most or differentially benefits, and which subgroup, not in a research study, but like in the real world, and which actually don't benefit. That can help inform the approaches to medical policy formulation.

There are many such conditions. They are in the areas of spine surgery, the areas of diagnostic imaging for lots of different conditions. I think there are many open questions around the relationship between the emerging science of genomics, personalized medicine and clinical application that lend themselves to study in the real world.

As an example, I heard a small research

study on whole genome sequencing and asking people at a cancer center where do you think the state-of-the-art of the clinical utility is of whole tumor sequencing, and half of the group in the cancer center said yes, I use this all the time in my clinical decision making, and the other half said I have no idea what to do with this kind of information in my clinical decision making.

Again, it may be a little early in that particular case, but issues with a lot of variation, lot of uncertainty for the clinical community and the need to study them in large numbers of real world settings. Those would be the criteria.

DR. NUSSMAN: If I may just build on Lew's point and add to Barbara's important question, the two studies that were selected, think about how we provide information. Low dose versus high dose aspirin. No one can easily track that. We don't have pharmacy data, we don't have claims, we have a personal engagement which will give us that answer.

Bariatric surgery, the nation is becoming

increasing obese. We are seeing that continuously. Obesity is coming attractions for diabetes, for cardiovascular disease. We all know that.

As Lew said, we probably don't see bariatric surgery as a solution to this public health dilemma, and most of us actually have created centers of excellence where they get great outcomes with bariatric surgery when it is covered, and we have basically answered that question, not to the extent that you are, but to our need.

The two that I would give you very specifically are two of the most important areas in health care today, and one is in cardiovascular disease. This is a good example of what I referenced. Now we have new therapies. We have PCSK9 inhibitors. We have statins that have been time honored. We have a 40 percent reduction in cardiovascular death over the last decade or two.

How then does this fit into the clinical profile of treatment and how does it fit perhaps even with interventional cardiology. That might be one where we have strong claims, real time

information on pharmacy.

The second is one that Francis and I were just commenting about briefly before we started, and that is all of the molecular diagnostics, all the molecular profiles, and how to best intervene in cancers based on that. That is again information. We as health plans as opposed to others support off label use of drugs if we think there is information or it makes some sense.

That is where I think a pragmatic clinical research and the detail we would have to inform and support and be research partners would be the greatest, in those two types of activities.

MR. BARNETT: Larry, Francis, and Joe. That is probably all we will have time for.

MR. BECKER: I want to go to process. We are going to have and are beginning to have research results. The normal process is you publish it in a journal. Do you on your end have a process to accept whatever evidence is out there, put it into plan design, put it in value based benefit design?

What can we do as we communicate these results to match up with your process, to facilitate that sort of marrying of these two processes?

DR. NUSSMAN: I can begin. We have, as you know, a very rigorous process that involves many external physicians, clinical researchers, scientists. We use many academic centers, and generally all health plans do this to a varying degree.

We accept that which is published, that which is presented at meetings, that which we learn about, we review it in great detail, and that's how we make decisions on both coverage and decisions on benefit design.

We really embrace the model of publication and peer review, but on the other hand, to be relevant today, we have to disseminate that information at the earliest possible time.

That's really what we want to do, and I think the good news is the medical journals and others have actually accelerated the time line for

very vital information to get out. That is the way we do it. I think the research of PCORI can build on that.

DR. SANDY: I think Sam said it well.

DR. COLLINS: I want to ask in context here, PCORnet, which has really remarkable capabilities emerging in terms of doing comparative effectiveness research with very large numbers of potential research participants, through the CDRNs and PPRNs, and now the emerging possibility of this precision medicine initiative of a million or more Americans who will be engaged in a longitudinal cohort study.

Under what circumstances would help plans like yours be willing to become engaged as a partner in terms of sharing data about those same individuals? It is all going to be about the various data types that can be assembled together in order to try to draw inferences about what helps keep people healthy or how their disease is best managed.

I'm sure there are all kinds of issues

there about privacy, confidential firewalls, but what would the criteria be for you to engage in a partnership and make those kinds of data accessible?

DR. SANDY: It's a great question. I think there are a number of different dimensions to the answer. I think the first one is there has to be -- you are focused on sort of scalable infrastructure. One of the barriers that I've seen is around sort of scaling up the infrastructure to do exactly what you said, particularly integration of data from clinical repositories, such as EHRs, and in the claims data.

I don't think it will work if every center has to kind of custom craft an approach working with every payer, and as I mentioned, we are part already of the FDA's Sentinel network. We were one of the founding contributors to a multi-payer repository called the Health Care Cost Institute.

Interestingly, originally built to just compile private sector cost trends relying not just on Medicare data for that view, but the same

repository has now been recognized, oh, we can actually look at other data, other questions, using a multi-payer claims view.

I think a scalable infrastructure, there are a number of regulatory issues that payers have to deal with regarding identified data as we are regulated entities, this is outside research, and I am aware of a number of different opportunities with individual academic health centers and networks, and we just couldn't pull it off because of privacy and security issues on the academic health center side. These are really kind of thorny technical regulatory issues that have to be addressed.

On the strategic level, there has to be a value proposition. There has to be something worthwhile that is worth the time and effort to go ahead and do it for all parties, including the payers.

DR. NUSSMAN: If I may just add to this, I think this is really important. We have been integral, meaning Anthem, United, in being

architects, shaping and contributing vast amounts of data to the Sentinel system.

Also what is important is we are strong participants with CMMI in testing models of care. There is a very important alignment across many dimensions. In fact, the White House has asked your question and we have responded that we will be part and want to be part of the personalized medicine initiative and will find a way of making that happen, whether it is rewarding clinicians to participate in oncology research or other models.

Here is one of the considerations that we have, at least at Anthem. As Lew and I have mentioned, we support many, many types of companies, and for those companies, we provide administrative services, but our base contracts say we don't pay for investigational and experimental therapies. That is the contract language yet we want to find that path to learn, to inform, so we can in the future pay for those services that are proven and remove waste.

That is in the contracts and that is why

we have found and looked for the strategy and tactics to get past that, such as entering a research project part of care coordination. There are many ways of getting there, but that probably, when you ask if there is an obstacle, that is the contract language that almost all health plans tend to have.

DR. SELBY: Lew and Sam, I want to first say thank you so much, this was richer than I think we anticipated. It was fantastic.

Both of you alluded to an issue that is relatively newly on my mind and on our minds. Sam talked about really recognizing issues in advance and getting out there with the research early on before practices are cemented. You talked about a rapid response strategy.

I think we are completely with you, and I think it was in the minds of the framers of the PCORI legislation that we would among other things support research into new therapies, new therapies where you really needed to understand how they compared with available therapies and in whom were

they really better. Classic patient-centered outcomes research.

One of the things we see is we essentially fund research that starts right after drugs are no longer investigational, drugs or other therapies. They are out there and available, at least in some places.

If we wanted to do a head to head study, head to head trial, of two competing new products in some particular area, we might find one of the industry sponsors of one of the products was very interested in the project but the other was not. PCORI is not in the business of paying for clinical services. We can't do that.

It would seem that payers and purchasers facing prospects of having to operate for a number of years without evidence might be willing to work in advance even on something appearing on the market so that we would have financing mechanisms if we wanted to compare two therapies or if there was some other kind of critical CER question that needed to be answered, that we knew even before day

one that we have at least the prospects of a mechanism for funding the treatment costs for both arms.

DR. SANDY: I would agree with that, Joe, and I think this is where -- it gets to Larry's question also -- I think what is really needed, and PCORI could really help do this, I talk to a lot of life science companies that are always trying to figure out kind of how do they address these issues, and I say what is really needed is speed to answer and speed to application, need to speed up the ability to answer the question.

They always want sort of product specific or company specific, inside into the question that we have, and I tell them the question, you know the answer to the question, you know the questions that we as a payer will have, how does something work in the real world, which patients, compared to what, how does

this new thing fit, most things aren't de novo treatments where there is no established therapy, how does it compare to existing standards of care.

That is a CER kind of question.

What are the outcomes that are most material to patients? Many of the innovations -- I want to emphasize what Sam said, too, we are interested in understanding and promoting high value innovation, and we mean high value as value for patients, how do we then figure out whether patients are really benefitting or not without doing this kind of thing.

We need to speed it up. That's my take.

UNIDENTIFIED: We really are on common ground here on what you suggest. We do this today. We do it in a real world evidence base. We look at two therapies. We are not just comparing the cost of two drugs. My goodness. We are comparing the impact of those drugs for asthma about emergency room visits or whether children are in school, or many of the more patient-centered quality of life and family issues.

We do that today so why not do that over a broader set of activities with other health plans and get to that answer much sooner.

DR. LEVINE: I'll be quick. You both alluded to the issue of eliminating low value care, things that are being done that have no benefit or have the potential of harm. I am just wondering, now we are on this long and winding path to payment reform, as we move toward alternative payment models, where pay for value, at least currently -- it's a long and winding road, I understand that.

As we progress down that road, do you think that task will be easy in terms of eliminating the instinct to continue to do stuff in the absence of evidence of benefit?

DR. NUSSBAUM: Payment reform, Sharon, I think is an enabler to greater velocity, get at waste and care that doesn't make a difference. The journey will be long and it will be tough.

In fact, Lew and I are both on the Guiding Committee that is looking at the framework for alternative payment models and value. In fact, we each chair a work group. Mine is the framework and the tracking. Lew can tell you more about his specific area.

We are personally very invested in this, but the real answer is that payment reform in and of itself is not a solution, it has to be an enabler for quality, for clinical performance, and to in many ways leave this nation head room for innovation. The real answer is getting rid of, as you know, the 30 percent waste so we can innovate new treatments and provide services to people.

DR. LEVINE: Do you think it will make the path easier?

DR. NUSSBAUM: I do; yes.

DR. SANDY: I think you get better alignment when you have advances in payment and you have more organized care delivery. It is helpful, but it is not going to drive it all by itself. There are a whole set of things that have to happen.

In some ways, it will make it easier, and in some ways it will make it more difficult. We can talk off line about that.

DR. KUNTZ: Lew, you talked about the need for a sales sheet. You alluded to sister agencies,

perhaps that was to AHRQ. We do have some experience recently with putting together sales sheets. We have kind of high on that sheet the observation that hospital care was 17 percent safer in 2013 than in 2010, 1.3 million fewer adverse events in hospitals, still 121 adverse events per 1,000 hospitalizations, well too many, but down from 145, 50,000 fewer people dying as a result.

As you noted, and Joe talked about a few early results, but it seems like a sales sheet today, much of what would be on it would be the anticipated result that would be coming later this year and next year and the next year.

The kind of question is whether you have any advice about how to frame a sales sheet in the context where there are some results to point to today but most are kind of on the cuff.

DR. SANDY: It's not my area of expertise. I majored in biomedical science. I would say even that comment is under clubbing what has already happened. I have tried to give you in my comments some thoughts around the value proposition that has

already been created and the promise.

You can sell a promissory note if people believe and it makes sense, yes, I'm willing to wait for that because that makes a lot of sense to me, that is worth waiting to see what happens. I think you are under selling it, Rick, if you just say you're a researcher, that's the way a researcher would think about it. I'm suggesting thinking about it differently, and there are other people who know how to do this far better than I do. I have tried to give some initial thoughts.

DR. NUSSBAUM: Rick, my only comment to add here is patient-centered, this matters a great deal to employers, to Government. The idea that patients can be more knowledgeable, can be partners in their care, share decision making, an area that you have focused a lot of the early grants on, this is incredibly important, and one of the areas that we have not excelled in, so the science, the patient-centeredness, and the shared knowledge has not moved in parallel, so I think that would be part of this compelling set of messages.

What is the real issue is this happens for NQF, those of us who have been involved with NQF know it happens, in these very complex technical domains, you have to make that compelling case and make it meaningful to everyone. Why is my life different today because of PCORI. You will find ways.

CHAIRMAN NORQUIST: Thank you, guys. You did a marvelous job, so thank you very much. This is not the end. We hope we have ongoing dialogue with payers and others. Don't think we won't call you again. Thank you.

[Applause.]

CHAIRMAN NORQUIST: We will now move into the next two sessions. You will see Christine and Bryan here for the next hour and a half. We are going to first consider the slate of proposals we have on Hepatitis C infection awards.

MS. GOERTZ: Thank you, Gray. We are excited to finally be at the point where we are talking about a proposed slate for our Hepatitis C initiative. Today we will be presenting two

applications that we are recommending for funding.

I just wanted everyone to know ahead of time that we are actually hoping there will be more applications coming. Staff are in discussions with other investigators beyond the slate we are presenting today. We are hopeful we will be bringing you additional awards for recommendation under the Hepatitis C initiative in the near future.

As you know, we have language in all of our funding announcements that say we consider a number of things when we are trying to decide what to fund, and there are a number of things that the staff and the Selection Committee look at before anything comes before the Board.

Obviously, a major part of that is the merit review, but another big part of that has to do with program priority and program fit. That is language that we have in all of our funding announcements.

The way that we are operationalizing it within the Hepatitis C slate is we are hoping we

will be able to fund applications within each of the four topics or questions, within screening, care management, head to head comparisons, and delayed treatment. Again, we are just going to be presenting two of those today.

We are a little bit behind schedule. I have asked Bryan to go as quickly as he can. Obviously, we want to make sure that we are able to answer all your questions. Bryan?

DR. LUCE: Thank you, Christine. These are the four questions. We're going to be talking about the care management and the head to head this afternoon. As Christine said, we are hopeful that we will have other opportunities in the near future for you to consider.

I have asked Steve Clauser to my left and Danielle Whicher to my right to be up here in case you want to drill in a little bit, although I do note we don't have a lot of time. Both of them have lived this for the past year actually.

The research question in terms of care management having to do with patient-centered

models of Hepatitis C care for people who inject drugs -- the question specifically addressed in this application is which Hepatitis C treatment delivery model for people who inject drugs is more effective for enhancing Hepatitis C treatment uptake, adherence, completion, virological outcomes, and reinfection.

This is a two arm randomized control trial of 1,000 people. They are Hepatitis C infected individuals who have used drugs within the past three months who will be recruited from 16 health centers in eight states, all with on-site Hepatitis C care, eight methadone clinics and eight community health centers.

The outcomes of interest here in terms of primary outcomes of sustained virological response - adherence, treatment completion, and reinfection, and secondary outcomes - quality of life, relapse, and complications of cirrhosis. The total budget for this study is just slightly more than $14 million.

This has extremely strong engagement as

does the other program that I'm going to introduce you to, the other application.

DR. LEVINE: When you say treatment delivery model, do you mean drug regimen or comparing health system organizations?

DR. LUCE: Health system organizations.

CHAIRMAN NORQUIST: What are the two arms?

DR. LUCE: The arms that are proposed in this study are patient navigation with peer support and direct observation of therapy either conducted in a methadone clinic or through a community health center. The community health center has options for patients to have that observation done in a variety of settings, either at the community health clinic, in a community setting of mutual agreement, or the primary care practice or at their home.

DR. LEVINE: There is no variation in the drug regimen, it will be the same drug regimen being deployed in different ways?

DR. LUCE: That is correct.

DR. McNEIL: What is the follow up?

DR. LUCE: The follow up period is 140

weeks.

DR. McNEIL: The reason I was asking the question, these are drug users, how do we know after 140 weeks they are not going to just pop back on and get Hepatitis again?

DR. LUCE: That is about a two and a half year follow up period. One of the discussions that came out of the Selection Committee is exploring the possibility of extending that period even a bit further, and should you agree this study moves forward, that is something we will definitely take up.

CHAIRMAN NORQUIST: Bryan, next.

DR. LUCE: The potential impact of the study is that results from the study will have the potential to drive programs serving these high-risk people who inject drugs.

With that, if I may, I will move on. The next study is a head to head study. It is called the Prioritize Study. It's a pragmatic randomized study of oral regimens for Hepatitis C, transforming decision making for patients,

providers, and stakeholders.

The research question, what are the comparative benefits and harms of three direct acting antivirals in adults infected with HCV in the U.S. population. This is an open label three arm RCT with just under 4,000 patients, adults in the U.S. diagnosed with Hepatitis C, genotype 1 recruited from 45 clinical sites.

The primary outcomes of interest are SVR12, sustained viral response over 12 weeks. Patient reported and clinically documented side effects. Secondary outcomes, treatment adherence, treatment persistence, out of pocket costs, amelioration of Hepatitis C symptoms, post-treatment progression or regression of liver disease, persistence of viral cure at three years post-treatment, and functional status during and after treatment. The total budget is $15.4 million.

Engagement includes Hepatitis C patient advisory groups, patient organization partnership committee that includes representation from eight

patient advocacy organizations. The potential impact here is providing decision makers with evidence about the comparative effectiveness and safety of these new direct acting antiviral drugs for Hepatitis C.

CHAIRMAN NORQUIST: Sharon?

DR. LEVINE: Same question, what are the three arms? What are the three measurements being compared?

DR. WHICHER: Harvoni, Viekira Pak, and the new Merck one to be approved by the FDA in January 2016.

DR. LEVINE: It would be helpful to have in the template a description of the different arms.

CHAIRMAN NORQUIST: I don't know why you couldn't tell us what the drugs are if we are going to fund it. I think in the future, let's make sure we have the arms so we know the interventions.

Is that it?

DR. LUCE: Yes.

CHAIRMAN NORQUIST: Before we have a

discussion, the following Board members have let us know about their intentions to recuse themselves from the discussion and votes on the awards for the clinical management of Hepatitis C infection. Debra Barksdale, Alicia Fernandez, Rick Kronick, and Harlan Krumholz. If there is anybody else, let me know now, please.

On the phone, I think we also have Harlan Weisman. Allen and Freda, I assume you are still on.

DR. DOUMA: I'm here.

CHAIRMAN NORQUIST: Freda?

[No response.]

CHAIRMAN NORQUIST: Harlan?

DR. WEISMAN: Yes, I am.

CHAIRMAN NORQUIST: Thanks. Now we are open for discussion.

DR. LUCE: You mentioned that we have extensive engagements with national organizations and so forth. I have a list of those organizations if you want to drill into them. They are quite impressive.

DR. COLLINS: What is the landscape of other studies of this sort that are being supported by other groups? I just don't know how this fits.

DR. LUCE: In terms of the head to head studies, there are no head to head studies that we're familiar with.

UNIDENTIFIED: In terms of the care management, for studies that are involving these brand new antiviral agents, there are no other studies that are currently underway to address this issue.

CHAIRMAN NORQUIST: Rick?

DR. KRONICK: Just to follow up on that question, what is the Merck study that is being proposed for approval? Do you know the structure of the Merck study?

DR. LEVINE: Merck has a multi-genome type drug in the pipeline and is likely to be approved.

DR. KRONICK: Was there a randomized control study that led to that?

DR. LEVINE: It is a drug that is in the pipeline, it has not been compared to anything

else. Merck has a drug that had an one year lag.

CHAIRMAN NORQUIST: They're adding one of the two that we have. We know this other one is going to be added at that point.

DR. LEVINE: The third arm is a drug that has yet to be approved by the FDA, but close.

DR. LUCE: This is a study that is projecting that drug will be available.

DR. KRONICK: The approval process for that drug --

DR. LUCE: It's not a comparison study, for example, Harvoni versus this new agent. It's not delivered in real world settings. It doesn't follow people for more than 24 weeks. It basically is powered by sustained viral response. It's efficacy studies. This is real world comparative effectiveness study after approval.

CHAIRMAN NORQUIST: Barbara?

DR. McNEIL: I want to ask a general question, Gray. I know the group that selects these grants for approval does an extremely thorough job. My concern is when we get to this

stage, I feel like I have no idea what I'm voting on and I have to take it completely on the face of the group that made the selection, and this is in fact a very pro forma vote. Should we have a more robust sense of what's being funded? I think Sharon was getting at that.

MS. GOERTZ: I think you bring up a really good question and it is something that we talk about at the Selection Committee and also I was on a conference call with the Governance Committee talking about conflict of interest.

In some ways, this all gets down to conflict of interest and how do we make sure we are addressing that appropriately.

Tomorrow, we will be cueing up a discussion where we talk about what role would the Board like to have when it comes to selecting what we fund and specifically do you have more clarity, to make sure the Selection Committee is doing the due diligence that you would want before it comes to the Board for recommendation.

DR. McNEIL: Just to be clear, Christine,

I wasn't asking for more due diligence on the part of the Selection Committee. I am going to assume they do the work. I was just asking what kind of information --

MS. GOERTZ: I wasn't clear.

UNIDENTIFIED: Could I just point out, Barbara, because I think this is a burning question in some people's minds, the Board has seen the questions in terms of after we had our stakeholder groups, we proposed a set of four questions including the two questions these studies address.

These studies then were competed through a funding announcement and a merit review panel, a peer review process, rated these studies highly. Beyond that, staff worked very hard on them to get additional information when needed and presented it to the Selection Committee, which actually had a fair amount of information about them on which to decide whether they looked like studies that could go forward.

At this point, the Board has still some lingering responsibilities but it is not to conduct

a third round of methodologic reviews. I think that has been accomplished. I think you still need to say whether there is something about this particular question as judged from the title that is objectionable. You need to say whether this amount of money seems appropriate.

I think you can't really submit applicants to triple jeopardy here. The Selection Committee is definitely a layering on of additional review and additional criteria.

It would also be very hard to do it in public or even in a day catch you up on the amount of information that the people who make this recommendation had at their disposal.

DR. WEISMAN: I agree with Barbara. I raised this previously. What I was told, Barbara, and I'm going to use my words, not necessarily the answer, but that it is perfunctory, that we have a fiduciary responsibility to approve budgets.

My feeling is if we come up with a method, can't we approve from the Board level a general area of research and then delegate the

responsibility for the specifics of how the money is being spent to the Selection Committee?

Otherwise, it is sort of a farce. I have no way of knowing on any of these, on any given presentation, whether these are good or not good research questions or research proposals. I am fully confident in the abilities of the Selection Committee to make those judgments. Are we really required to bring these to Board vote? It's sort of a silly exercise.

CHAIRMAN NORQUIST: We are going to have more discussion. We are trying to do it with the Governance Committee. I think what we are operating on as I said earlier, Francis, what we said earlier.

DR. COLLINS: I think what would help with this, if I could make a suggestion, I do think we need to make decisions at the Board about funding, maybe hear a little more from the Selection Committee about the conversations they had. That was sort of missing here. We saw here are the two that are being proposed.

Christine, I don't know if you can do this off the cuff or maybe for the future if we just had that snapshot, that is a group that we trust that has expertise. I think it would be helpful to the Board to hear what were the conversations you had about the pro's and con's of what was put in front of you and why did you come down the way you did.

CHAIRMAN NORQUIST: I think that would be helpful. I think that would alleviate some of the concerns people have. Christine, maybe you can help with that.

MS. GOERTZ: I agree completely. I would have a little trouble doing that off the cuff right now. I don't have my notes in front of me. I would just hate to misspeak. I think that is an excellent idea and I am committed to making sure we do that in the future.

CHAIRMAN NORQUIST: I do know in this case that a couple of the people involved are recused now, and I know you guys went a lot back and forth on these, and there are other applications that are still undergoing some further review that are not

being presented, four of the other two topic areas, so these are the only two that have been brought forward after much discussion.

MS. GOERTZ: Right, that's exactly right. These were not the only applications that were presented to us for consideration but these were the only ones we felt comfortable with moving forward with until we had more information.

CHAIRMAN NORQUIST: Leah?

MS. HOLE-MARSHALL: I would just add generically that for those of us who could vote on the Selection Committee, these two were unanimously approved to move forward with a recommendation to the Board.

MS. GOERTZ: Right, absolutely. That, I could have done off the cuff.

CHAIRMAN NORQUIST: Okay. Any further comments? Allen?

[No response.]

CHAIRMAN NORQUIST: What I need now is a motion to approve the funding of these two particular awards. That is what we are approving,

the funding.

UNIDENTIFIED: So moved.

UNIDENTIFIED: Second.

CHAIRMAN NORQUIST: I'm going to have people in the room hold up your hands if you are in favor of funding these two awards.

[Show of hands.]

CHAIRMAN NORQUIST: Anybody opposed? Anybody abstaining?

[No response.]

CHAIRMAN NORQUIST: On the phone, Harlan?

DR. WEISMAN: I support it, I vote yes.

CHAIRMAN NORQUIST: Freda?

[No response.]

CHAIRMAN NORQUIST: Allen?

DR. DOUMA: I approve.

CHAIRMAN NORQUIST: It passes. Thank you very much.

The next topic is one where we are going to discuss two targeted funding announcement topics, basically. We are going to be talking about the one we brought back, which is the issue

about opioid misuse and how we deal with that, and then multiple sclerosis, which we will consider separately. I want to have them discussed as separate items, not as a package.

MS. GOERTZ: Bryan, are we going to start with multiple sclerosis first?

DR. LUCE: We will start with multiple sclerosis. I am going to go through this very quickly because --

CHAIRMAN NORQUIST: We are back on schedule now. We want to leave room for discussion.

DR. LUCE: Just to remind the Board, this is the pathway to a funding announcement, this is what we are talking about, a funding announcement and a commitment to a funding announcement. It is really quite a long process that deeply involves staff and involves stakeholder groups and the advisory panels of the different research programs that we have, and the SOCs involved throughout, literally throughout.

Reviewing the initial topics that come

into us from various stakeholders, which in essence is this list one, and it goes to list two, and it keeps getting refined until we are before you making a recommendation for an announcement, just to give you a sense of the intensity of the process.

We have already approved 10. The most recent ones were the new oral anticoagulants and treatment-resistant depression, that I'm sure you are familiar with.

For today, as Gray just mentioned, we have long-term opioid treatment for chronic pain, treatment for MS. I will start off with MS.

Also, soon to come up to you likely is chronic low back pain and integration of mental health into primary care in diabetes.

DR. LEVINE: I just wanted to clarify, the topic brief presentation, does that include the literature review on the topic?

DR. LUCE: The answer is yes, but it is a brief, it is not a formal systematic review.

DR. LEVINE: It's not an evaluation of the

quality of the research?

DR. LUCE: It's an evaluation of the quality of the research and what the gaps are. That typically goes to the advisory panels for review and comments.

MS. GOERTZ: It is a summary of the evidence and an overview of sort of the state of the science. If you would like to see one, we could make that available.

DR. LUCE: I'm going to skip to treatment of multiple sclerosis. I have asked Diane Bild to my immediate right to be available in case you want to drill into any particular questions. Diane has been following this and shepherded this all the way through for a long time.

As you all know, multiple sclerosis is a chronic degenerative condition of the central nervous system characterized by damage to the myelin sheaths of nerves resulting in fatigue, numbness, visual disturbances, bladder problems, mobility difficulties, and other symptoms. It is really a very challenging disease for approximately

400,000 Americans. Most patients are diagnosed between 20 and 40 years of age, and a great deal of them are female.

The clinical course is highly variable, it generally unfolds over decades, and symptoms range from mild to the development of very severe disability.

There are three approaches to MS treatment disease modifying therapy to slow progression; steroids for relapses, and symptomatic treatments for specific symptoms of the disease and side effects of treatment regimens.

Over a long clinical course, symptoms that affect quality of life are life long. The DMTs, the disease modifying therapies, are used in patients with relapses or inflammatory activity. However, there is little evidence to support specific DMT choices or strategies. There are many symptom specific medications that have not been well evaluated or compared. That is true with respect to the DMTs themselves, in terms of having them directly compared with each other.

In April, we had a multi-stakeholder work group. It included 43 participants. You can see the breakdown in the multi-stakeholder work group in terms of where they came from. They grouped themselves or we helped group them into four different categories - comparisons of DMTs, including differential effects in subgroups, care strategies, non-DMT and non-pharmacologic therapy for specific symptoms and overall health and timing of therapy and study design. Each one of these areas were addressed in terms of what are the appropriate questions that we may be interested in addressing.

In terms of the need for better evidence through all of this process, and it does include a topic brief, the Canadian Agency for Drugs and Technologies in Health, CADTH, in 2013 noted a limited number of RCTs directly comparing DMTs for relapsing-remitting MS.

There were 17 systematic reviews that indicated insufficient evidence of treatment of MS symptoms, and a recent systematic review on tele-

rehabilitation for patients with MS concluded there is a need for more robust trials.

We have been dealing with this issue for a while now, having a very difficult time trying to figure out what exactly we could do to improve the evidence base.

The three questions that we are proposing be part of this announcement are first, what are the comparative benefits and harms of different DMTs or therapeutic strategies in patients with relapsing-remitting MS on symptoms, functioning, quality of life, disease activity, and disease progression.

Population of interest would be patients with relapsing-remitting MS. Comparators would be different DMTs, including strategies for sequencing or combining agents, changing to a different DMT or escalating DMT dose. Outcomes would be symptoms, functioning, quality of life, disease activity, disease progression.

We are proposing this to be in an outpatient setting, an RCT of five years, proposing

to commit up to two studies, $30 million in total costs.

The second question is what are the comparative benefits and harms of different approaches, other than DMTs, for ameliorating important symptoms in people with MS. Symptoms of interest include -- you can see all of these particular symptoms, which is substantial.

The population would be patients with MS, including progressive MS. Comparators would be non-DMT symptomatic therapies. Outcomes would be symptom relief and quality of life. Again, this would be an outpatient study. An RCT of over three years. We are recommending a commitment of $10 million for up to four studies. $10 million in total costs.

The third and final, in people with MS, what is the comparative effectiveness of tele-rehabilitation versus conventional direct care interventions for improving outcomes in people with MS, such as functional status, fatigue, and quality of life.

These would be patients with MS including progressive MS. The comparators would be conventional direct care versus telerehabilitation. Outcomes would be functional improvement, fatigue, patient experience, health related quality of life. Again, this is a randomized control trial over four years, and we are proposing to commit $10 million for up to two studies.

Those are the three questions of interest. Diane is here if you have particular questions you want to address.

CHAIRMAN NORQUIST: Larry, and then Gail, and then we will get to the people on the phone.

MR. BECKER: Go back to question number one, the two studies for $30 million.

CHAIRMAN NORQUIST: Larry, you need to talk into the microphone.

MR. BECKER: Sorry. Two studies, up to $30 million. How did you come to two studies would be enough and $30 million ought to cover this question?

DR. LUCE: That is definitely a Diane Bild

question.

DR. BILD: Yes, thank you. There is sort of a sub-bullet. We were thinking of two different approaches. One is what is the initial approach to treating MS with DMTs, and the second general question is what happens after you have failures, so to speak, with your initial DMT, how do you choose the second line therapy.

We listed a number of different strategies in terms of how the medications could be chosen or a change in their dose, et cetera. That would be left up to the investigator.

CHAIRMAN NORQUIST: Did that help?

MR. BECKER: It is really complicated and just two studies feels like -- I don't know.

DR. LUCE: It really is complicated. The outcomes take a while to observe. There are 12 drugs. There is a wide practice variation right now.

Diane laid out two of the crucial decision points. One is which agent makes the most sense to start with, and does that differ among subgroups of

patients with the condition.

The second question, a very different question and a different study population, as Diane just laid out, in people who have failed the first therapy, where do you go next. Do you add a therapy. Do you substitute a therapy.

Those two questions are distinct, those are the two questions that clinicians and patients have told us we should really get started on, and because these studies have outcomes that take a while to occur, you need a fairly large sample size in a period of time.

MR. BECKER: I'm not quibbling with it's the right thing to do. I'm just trying to figure out how did we figure out how much and how many studies.

DR. LUCE: The two studies were because there were two distinct questions. That is why we have two studies. Two equals two. The other point about the samples, I'm pretty sure, Diane, that we did do some sample size calculations. In fact, didn't we even engage someone to do some sample

size calculations for us, and to which we applied cost estimates?

DR. BILD: Right.

CHAIRMAN NORQUIST: All this is hypothetical. We will see what kind of research studies come in. Somebody may be creative and come in for $20 million. We will see what we get. The real interest is going to be what comes in under this question, to be quite honest.

DR. LUCE: Did you have an alternative suggestion, Larry?

MR. BECKER: I do know when you make it more and more complicated, you try to break it down in bite size pieces so you can compare these two things and then those two things, rather than -- I think I heard you say there were 12 different things here.

DR. BILD: The 12, a little bit more of the details that the clinicians will understand. It's not that any of the 12 is used as initial therapy and they are all equal for the next step. Again, we would rely on the real experts, the

investigators out in the field, to craft the appropriate questions under these parameters.

DR. LUCE: This is an inexact science for sure. There is very little if any head to head studies on these products.

CHAIRMAN NORQUIST: Gail, and then Rick, and then the two Bobs.

MS. HUNT: What is tele-rehab?

CHAIRMAN NORQUIST: It's the third question, I was going to ask, too.

MS. HUNT: Just generally, when you say tele-rehabilitation, could you describe what that is that you had in mind?

DR. BILD: I'm also gesturing to one of my colleagues, Steve Clauser, who worked up this question. It has to do with therapies that are delivered remotely in general.

MS. HUNT: I know that part. I meant something more specific. I know what tele-medicine is. I'm at a loss of what tele-rehab means.

DR. CLAUSER: I just wanted to comment there are a few of these types of interventions

that have been studied in much smaller trials using a lot of web based interfaces between the individual and remote experts who can actually work them through these particular rehabilitation therapies, and then kind of monitor that and communicate back and forth with their primary clinicians on that particular intervention.

CHAIRMAN NORQUIST: Is this a comparison of like providing it in person or providing it by tele-health connection or is it an unique intervention that is provided by the tele-health connection?

DR. LUCE: I'm not exactly sure I understand your question. Could you clarify it?

CHAIRMAN NORQUIST: Some questions are simply if I do this in person, if I do it by a tele-health connection, is it the same, do you get the same results as if you did it in person. That is simply the comparison of the technology, if you will.

There are other questions that focus on is it something unique like if you broadened the term

"tele-health," you get into social networking and other kind of things like that you could do that are actually unique interventions that are delivered over the technology that can be compared in another kind of way.

If that's the question, that's completely different than the first question, which simply is comparing in person versus the technology from a distance, which quite honestly, if that's the question, that's a question that has been answered 100 times, I think, and that is what I'm trying to get at here.

Is that what you are testing or something unique that you are delivering by this technology?

DR. LUCE: There are a couple of things that are unique. One is that a number of the studies that have been done regarding MS have largely been done with specialty centers, looking at specialty center direct care versus specialty center remote delivery.

This is looking for individuals that do not have access to specialty centers, where there

are real evidence gaps about how to deal with these patients that are in communities or in rural areas that don't have access. It is dealing with the population issue, which really hasn't been studied in this area effectively.

The second question is they are comparing specific modalities against one another, using either a tele-health approach or not. Those comparative studies have not been done to the standpoint where they can demonstrate to patients or at least for some subset of patients which one of these is really the most effective in terms of their ability to achieve their functional objectives regarding issues related to rehabilitation.

DR. KUNTZ: At the risk of re-litigating because we did discuss this in the SOC, the timing seems tough. Question two is trying to figure out which approach, DMT approaches, actually will work. By asking question two, I think we are saying we don't really know that, and we had this discussion in the SOC for people with secondary progressive,

where I think there is missing information about is there anything that will work to alleviate symptoms and help people with walking, et cetera.

Not yet having answered that question, it then seems very difficult to figure out what we are going to do on question three, which is will this stuff work as well or better if we do it remotely as if we do it face to face.

I'm still kind of struggling with that piece.

UNIDENTIFIED: My understanding of the tele-health question is about people who don't have access to MS centers, which is a lot of people. It is less about the use of novel therapies, which as you point out we have yet to have evidence around, and more about the use of the expertise available at an MS center.

Let me give you an example. MS person is in a wheelchair or perhaps has problems with bowel or bladder control. Access to a nurse who can help with that via tele-medicine, without having to undertake this enormous trip to go and see someone

for 15-20 minutes, might be extraordinarily valuable for that patient.

Or for example, physical rehab, going to a rehab center, you learn to do the exercises, you go home, can a physical therapist deliver via tele-health, can they see enough, be safe enough, be helpful enough to be able to actually help the patient see whether or not they are doing the exercises correctly and can gain more strength.

What I'm saying is when you go to one of these centers, as you know, there is an accumulation of expertise and a lot of little, meaning not which drug is going to change the course of the disease, but a lot of the things that greatly affect the quality of life for patients with these conditions.

To me, this seems like a very reasonable question. I don't know what the investigators will come up with in terms of what they will be looking at, nursing access, physical therapist access, physician access. It is useful to know whether these centers of expertise can communicate remotely

with the patient in a way that is actually useful for this often heavily incapacitated, heavily immobile patient population.

Did that help?

DR. KRONICK: It does, but I think the answer presupposes kind of the answer to question two, which is if what these centers are doing is actually helpful. I read question two in part as asking that, or at least what pieces of what the centers are doing is helpful.

I think for secondary progressive, as far as I'm aware, we don't really know that. It's a little bit tough to then ask which pieces of it can be done remotely when there is still missing information about which pieces of it are helpful when done in person.

UNIDENTIFIED: No, I don't see it that way. I think you are right that there are many aspects of things that are being done that we don't know yet, how efficacious they are, or if they are efficacious, is one more efficacious than another.

I think there are many things that we

actually do know that is accumulated through experience and expertise in those centers. Certainly, when I have had colleagues/friends who have MS, I have said go to an MS center, it's not so much the physicians you want, it's the nurses. They will help you. They will figure it out. Having access to those people in terms of living your life in a day to day world can be extraordinarily important, notwithstanding all unfortunately that we have yet to learn about these diseases.

For example, exercise is one that would fit into this category.

CHAIRMAN NORQUIST: If you go in person, you are assuming that, I am still wondering if going to the centers in person -- it may depend on the center you go to, for that matter, which may be unique. I don't know if that question is answered if you then start looking at whether it is delivered over a tele-health connection, okay, but first I would want to make sure that even in person I'm getting an added benefit, more than going to my

GP.

Allen, I know you have a question. I have Bob Zwolak first and then Bob Jesse.

DR. ZWOLAK: Thank you. We have spent hours discussing this very complex subject on the SOC. I learned a lot.

CHAIRMAN NORQUIST: Which complex subject?

DR. ZWOLAK: All three. I learned a lot about this, but would like to make a comment about three and a question about one. The comment about three is in a way I see this as perhaps the most patient-centered question of them all, especially coming from a rural area, which is two and a half hours from one of these centers, it's very, very helpful if the established therapy could be delivered effectively by tele-health.

Having said that, I realize it is sort of a theoretical contradiction with two, but I think three is really important. I think we do know enough about treatments to test tele-health.

The question I have to Diane and Bryan about one was this is a follow up to what Larry

said, there are two limiting parameters here. One is up to two studies, up to $30 million. My suspicion is the studies will come in at high dollar bids because they are complex studies.

Why would we sort of arbitrarily limit this at two, if someone came in, three people came in with high quality $10 million studies, would we refuse one of them? I'm wondering if two is not potentially an artificially limiting parameter.

DR. LUCE: I guess my answer to that is we still have the freedom to maneuver, it doesn't constrain us, I don't believe.

CHAIRMAN NORQUIST: You're going to get more than two applications, probably, we hope. You could get four applications. What we are saying is $30 million is probably a cap on the budget, but we will see. It could be that we want to spend $35 million if we really have three great studies. I think it will depend on what we get.

DR. LUCE: We are actually asking for approval of $50 million total. That is to answer the other questions, too.

DR. JESSE: My concern, and I am going to sort of ask the same question Rick did in a different way, we don't spend $50 million to be yet another study and systemic review that doesn't answer the questions that need to be answered.

From the perspective of the Board, it would be very useful to hear that the endorsing committees really believe these are the fundamental unanswered questions, and that supporting these studies is really going to meet a very fitting need.

As Larry said, we would be breaking it down into much smaller soluble units, which some of this is, particularly around tele-health and the like. Are we certain these investments will actually answer from the patient's perspective those pressing needs and not just contribute to another little chunk that doesn't fundamentally get to the root of the problems.

CHAIRMAN NORQUIST: Bob, I think you chaired the particular committee that discussed this topic.

DR. ZWOLAK: I chaired one of the three or four sessions we had about this.

MS. GOERTZ: I think all of you are bringing up a good point in that in the future, we can give you a better and more comprehensive recap of what the discussions are. We have the notes. We actually have pretty good notes from all of these meetings and we would be able to start off all of these discussions, both with the Selection Committee and with the SOC, about what was the nature of the discussion, and why it was in the end we felt strongly about moving forward.

UNIDENTIFIED: That actually starts the discussion at the Board at a very different place.

CHAIRMAN NORQUIST: Yes, I think that is a good point. Allen?

DR. DOUMA: I have two questions. The first one is are we going to have any arms of any of these three areas where the person is not taking a DMT either because they were assigned a placebo or otherwise?

My second question, Joe, I think you

talked about we are going to be looking at what do you do after failure, which is one of the challenges in this area, defining failure. Are we proposing we are going to do that for the researchers or are they going to do that for us?

DR. LUCE: The answer to the first is no, we're not going to have a placebo arm.

DR. KUNTZ: When we discussed the second study, there was discussion about the importance of having a study for people with secondary progressive and in full disclosure, my wife does have secondary progressive, so I'm not disinterested here, and most people who are secondary progressive or many people are not on disease modifying therapy.

There was even some discussion on trying to focus that question entirely on people with secondary progressive, and I know that is not where we got here.

There would be, I think, correct me if I'm wrong, substantial numbers of people in this study who were not on a DMT, it is not a placebo arm, to

Allen's question.

DR. DOUMA: Even with relapsing-remitting, and I have a conflict there, I guess, do we feel comfortable enough to know that somebody, a huge percentage of people, are not taking any DMTs, don't plan to take any DMTs, do we think that has been solved, they should, or we going to just try to not go down that pathway because it gets too complicated?

MS. GOERTZ: I may have lost track of the questions, but there was a question about whether we would entertain placebo-controlled studies, and I think Bryan answered that.

There was a question that if somebody was not on DMTs, would we encourage their use. That is the way I heard it. The first question here is on the strategy for prescribing and using and choosing among DMTs. There was also a question about how we would define "failure." We would not make that definition for the investigator. We would expect they would come in with their proposal with a valid definition of "failure."

UNIDENTIFIED: The proposed research question one is what are the comparative benefits and harms of different DMTs or therapeutic strategies. Might one of the therapeutic strategies that an investigator proposed be not using a DMT for someone with relapsing-remitting.

MS. GOERTZ: The wording of that question was meant to be not just the choice of the DMT but whether it was a combination or the dose or the strategy. We will start with one and then we will go to another.

I think if somebody came in with that kind of a proposal and it fits the question, we would consider it.

UNIDENTIFIED: Are we talking about slightly modifying the question then to make it more clear that would be one comparison that would be acceptable?

MS. GOERTZ: We can work on that.

CHAIRMAN NORQUIST: Harlan?

DR. WEISMAN: I don't have any new questions. I think this is one of the most

important therapeutic quagmires we have. Effective treatment for multiple sclerosis, which is a complex condition with many different forms, it is daunting just listening to the discussion.

On the other hand, I feel it is important for PCORI to tackle this, and my view is all the things we have talked about are really important, but it is going to come down to what are the specifics of the research proposals that are sent to us.

I imagine what sounds like was a challenging discussion in the committee, it will be even more challenging when reviewing actual submitted applications. I think we have to just go forward with it and not shy away from it because it is so important and so complex, and whether we take the kind of approach that Larry was advocating or some other approach, I guess I would leave to the wisdom of the committee.

CHAIRMAN NORQUIST: We are getting a little behind on our time. I think we all agree with that. Nobody is disagreeing that the topic is

not important. It is just the parameters around each of these questions, I think. Indeed, I think it is going to depend a lot on what kind of proposals. We may get zero proposals. We will see.

Any further discussion about this particular topic?

[No response.]

CHAIRMAN NORQUIST: What I need is a motion to approve issuing this targeted funding announcement for multiple sclerosis for these three questions.

UNIDENTIFIED: So moved.

UNIDENTIFIED: Second.

CHAIRMAN NORQUIST: In the room, I need people to hold up their hands if you are in favor.

[Show of hands.]

CHAIRMAN NORQUIST: Anyone opposed in the room? Abstaining?

[No response.]

CHAIRMAN NORQUIST: On the phone, Allen?

DR. DOUMA: I approve with the caveat that

I hope we incorporate a lot of the conversation, including my conversation about this.

CHAIRMAN NORQUIST: I think they will. You approve. Okay. Freda?

DR. LEWIS-HALL: Approve.

CHAIRMAN NORQUIST: Harlan?

DR. WEISMAN: Approve.

CHAIRMAN NORQUIST: It passes.

UNIDENTIFIED: I voted to approve. I would like to make one last comment. I still think there is likely to be much more value from questions one and two, and as the applications come in, I would hope the Selection Committee would look carefully at that, if there is a compelling argument from an applicant on question three, that it makes sense to go forward, but it still seems like a logical problem that if we don't know from question two what is really working, how we are going to do question three.

CHAIRMAN NORQUIST: I agree. I think that gets into the weight of what we want to put on each of these questions.

Let's move on, clinical strategies for managing and reducing long term opioid use for chronic pain.

DR. LUCE: I just want to note we chose MS first because it was going to be so easy.

CHAIRMAN NORQUIST: We do have a break scheduled. We have to take a break at some point here.

DR. LUCE: The Board will remember that we brought this to you in the last meeting. I won't go through the whole discussion by any means. I want you to know the staff listened very carefully. They discussed the issues that were raised with specific Board members that had issues and had ideas, and spent some time talking with the National Institute on Drug Abuse, NIDA, about these issues as well. They reformulated the questions.

Layla Lavasani is to my right in case you want to drill down into specific issues.

Quickly, the overview, you have seen.

CHAIRMAN NORQUIST: Christine, did you want to say something?

MS. GOERTZ: The SOC paid a lot of attention to the discussion that occurred during our Board conference call. We went back. There was a lot of intense conversation following on that discussion about what to do. This is an area where everybody is not necessarily in complete agreement, but I can tell you that all of us felt very comfortable with where we ended up finally with this particular funding announcement.

UNIDENTIFIED: One comment that came up at the last meeting was whether we had checked these particular questions out with substance abuse research experts, particularly those at the National Institute for Drug Abuse. We did, including a really nice conversation with Dr. Volkow, the Director of NIDA, and two other persons.

They said the two questions here are different and extremely important from their point of view. We did identify a third question which may be the topic of a future funding announcement about primary prevention of opioid use.

These two that are put forward today have ringing endorsement from NIDA.

DR. LUCE: Do you want me to cut right to the chase?

CHAIRMAN NORQUIST: Yes.

DR. LUCE: These are the two proposed questions we are putting forth to you. The first deals with the comparative effectiveness of strategies to reduce or to eliminate opioid use while managing pain, and the second is the comparative effectiveness of strategies to prevent dose escalation.

I think both of those questions are directly related to the concerns that Sharon and others shared.

DR. LEVINE: In our conversation, and I think even in the general conversation about this, it is important that we qualify this to reduce or eliminate opioid use while managing chronic non-cancer pain.

DR. LUCE: That's correct. That is true with both of them, both non-cancer pain.

Among patients with chronic non-cancer pain, moderate to high dose long-term opioid therapy, what is the comparative effectiveness of the strategies for reducing or eliminating opioid use while managing pain. You can see the strategies.

The population is patients with chronic non-cancer pain on high dose long term opioid therapy, the comparatives may include structured opioid dose reduction versus opioid dose reduction combined with non-opioid interventions. The outcomes are pain control at six and 12 months, opioid dose reduction or elimination at six to 12 months, and functional status, quality of life, opioid misuse, safety, mortality, medical side effects of treatment, depression score, hospitalizations, and other health services.

We are proposing the study would have a greater than one year follow up, an RCT of three to five years. It would be a subgroup analysis, how does effectiveness vary based on patient comorbidities, mental health disorders, past or

current substance abuse disorders.

Do you want to discuss this before I go onto the next question?

CHAIRMAN NORQUIST: Why don't you show us the second question.

DR. LUCE: The second question, a lot of it is very similar, except we are talking about different patient populations slightly.

Among patients on moderate to low dose long term opioid therapy, what are the comparative effectiveness of harms and strategies used to limit dose escalation. The population is chronic non-cancer pain but on moderate/low dose long-term opioid therapy.

The protocols and the comparatives would be the protocols to limit those escalations versus standard risk mitigation strategies. Comparisons may include strategies of non-opioid interventions or opioid rotation or dosing strategies or other risk mitigation strategies.

The outcomes are pain control at six and 12 months, opioid dose at 6 and 12 months, quality

of life, opioid misuse, safety, mortality, side effects of treatment, and depression score, hospitalizations, and other health services.

This would also be a study that is over an one-year follow up, RCT over three to five years. The potential subgroup analyses, how does the effectiveness vary depending on patient comorbidities, such as mental health disorders, past or current substance abuse disorders, and the type or cause of pain.

We are proposing to commit for these two questions up to four studies, $40 million total cost.

DR. KUNTZ: First, these are really important questions, like MS. I just wondered when I look at the variable you have here, should we be thinking more about portfolio studies. A single study is not going to answer the question, it is going to be a group of studies. I wonder if we can think on the MS side, too, to say maybe we can think about a structured set of studies that would really answer the question together and give a

little bit of guidance.

DR. LAVASANI: One of the things we talked about was the outcomes for research question two would be at least 6 and 12 months. In terms of further defining what high, medium, and low dose is, we would have further discussion about whether it could be consistent with the CDC recommendation or that researchers indicate if they are not going to be consistent, why that is, and to have that information available for us. There is broad variation in how people define those terms. I think we want to be consistent.

MS. GOERTZ: I think what we were thinking about is high dose versus moderate dose, there are different measures. CDC, of course, uses particular measures. We thought about defining high dose within the funding announcement as 120 milligrams morphine equivalent dose per day, that has become the Washington State's guideline. We do understand that varies, and we would give investigators options to provide justification for the thresholds they will use.

UNIDENTIFIED: I do think we should consider consistency with the CDC guidelines because this is a Federal platform. Because it varies by state, I think using a national standard -- while we are not a national agency, being more consistent with that would be helpful. I don't think we would have to require it. We could say this is where we would like individuals to start, and the researchers could let us know if they felt it was appropriate to have a different standard.

CHAIRMAN NORQUIST: That's a good point. If they wanted to make an argument of why they didn't want to use that, we should consider that argument. Yes, I think that is a good idea.

For the people on the phone, we don't have any other comments here. Do you have any questions?

[No response.]

CHAIRMAN NORQUIST: I think you guys did a wonderful job of coming back with the questions revamped and reorganized and listened to the concerns, so thank you very much for that.

UNIDENTIFIED: I do feel very strongly, so I just wanted to make that statement here that we don't have a question on primary prevention that should be on the table, there has been a commitment with staff to at least investigate whether that possibly could occur.

I appreciate these questions and I think they are very important.

CHAIRMAN NORQUIST: We should make it clear that there may be a third question. What we are asking for now is basically on these two questions, so I need a motion to approve this potential $40 million.

UNIDENTIFIED: So moved.

UNIDENTIFIED: Second.

CHAIRMAN NORQUIST: In the room, if everybody would raise their hand who is in favor of this.

[Show of hands.]

CHAIRMAN NORQUIST: Opposed? Abstaining?

[No response.]

CHAIRMAN NORQUIST: On the phone, Allen?

DR. DOUMA: Approve.

CHAIRMAN NORQUIST: Freda?

DR. LEWIS-HALL: I do.

CHAIRMAN NORQUIST: Harlan Weisman?

DR. WEISMAN: Approve.

CHAIRMAN NORQUIST: Francis Collins before he left said he approved. It passed unanimously. Thanks. With that, we have about a 15 minute break. Thanks.

[Recess.]

CHAIRMAN NORQUIST: Let's get started now. For those of you on the phone, the next session is an update from the Methodology Committee. What we are doing now is adding five minutes, so you have until 4:05 as opposed to 4:00. You are stopping at 4:05 now instead of 4:00.

Robin Newhouse, who is the chair of our Methodology Committee, will give us an update on the Methodology Committee. I think Steve Goodman has also just arrived, but is probably tired from his trip. He is here as the vice-chair. Robin?

DR. NEWHOUSE: Thank you, Gray. We are

delighted to present an update to the Methodology Committee's work since the last Board meeting. On behalf of the Methodology Committee, I'm Robin Newhouse, here with Steve Goodman, vice-chair, of the Methodology Committee. I'd also like to note that we have a couple of our Methodology Committee members on the phone who will be recording a portion of the update, and I'll introduce them in just a minute.

Today what we will cover is an update on some of the decision sciences work that we have started, actually about a year and a half ago. We will also talk about our major work in terms of developing new methodology standards, those are designs with clusters and complex interventions.

We will also update you on the revision of our first standards that were first presented in 2012, and started their use in proposals in 2013. It's hard to believe they are about three years old and they have now all been revised with the help of the PCORI staff. We will update you on that work as well.

We will end by talking about some of the methodology standards dissemination activities, that is the continuing education and academic curriculum.

That is what we will cover. At the end, we will update on a couple of additional issues. That is where I am going to ask for Sally Morton to tell us a little bit about her work in the PCORnet methods subgroup as well as some of the simulation model subgroup work that she has led.

In terms of decision sciences, this emerged actually a couple of years ago as an interest to try to understand where PCORI should be in terms of their space in decision sciences. A subgroup of Methodology Committee members and PCORI staff worked with the Research Triangle Institute and held an expert workshop on June 4.

As a result of that work, they completed a report and summarized the evidence. We have not yet seen the report. It will be distributed among the Methodology Committee and it will be posted publicly, and the next steps are to come.

In terms of methodology standards, over the past year, the Methodology Committee has worked on two standards that were important to core methods. Those were designs with clusters --

MS. HOLE-MARSHALL: Sorry, can I ask a question about the previous slide?

DR. NEWHOUSE: Sure.

MS. HOLE-MARSHALL: Can you just give me an example of decision sciences type, what the report covers in terms of maybe just an example, is it study methodology, it is application, or both?

DR. NEWHOUSE: Yes. In anticipation of that question, I'm going to call Bill Lawrence because he was involved, and actually Steve and I have not yet seen the report. We had a brief report from the Methodology Committee members that the work was complete but not sort of the dense findings and the recommendations to move forward.

DR. LAWRENCE: Hi, I'm Bill Lawrence with the Communication Dissemination Research Program. The meeting basically focused on decision methodology primarily, so it was decision

psychology, behavioral economics, with a lot of focus on choice architecture, and sort of the ethics of decision-making, kind of the primary areas involved. I'd be happy to go into detail if you would like.

MS. HOLE-MARSHALL: Basically how people make a decision, in particular in this case, about a health care choice that might be in front of them.

DR. LAWRENCE: Correct.

UNIDENTIFIED: Thank you.

DR. NEWHOUSE: Thanks, Leah. In terms of the new methodology standards, the work for design with clusters is complete, and the steps that we went through to develop the design with clusters standard included a conference back in June with experts. They actually came to the conference, the work shop, with some recommendations for standards for design with clusters and to work with PCORI staff, and the subgroup from the Methodology Committee refined those recommendations.

The recommendations were then presented to

the Methodology Committee and modifications made, and now they are ready to be reviewed and voted on by the Methodology Committee. We have a face to face meeting in October, October 29, at which time we will be reviewing those recommended standards and voting to have them ready to bring back to you for your review for the December meeting before they are publicly posted for comment.

MS. HOLE-MARSHALL: Robin, this one, what will come to us is proposed standards to get public input but then after that, at some point they would be adopted as methodology standards. Is that the intent?

DR. NEWHOUSE: Yes, they would be added as another new methodology standard and will go through the same process as we did when we presented the first standards, it comes to you, it goes out for public comment. We will incorporate all public comments into the standards, and then they will be endorsed, hopefully, by the Board, and then will be used in proposals.

MS. HOLE-MARSHALL: As opposed to the

earlier one about decisions, that one is not moving towards standards or until you get the recommendations, you won't know?

DR. NEWHOUSE: That conversation about decision sciences has been one that we have been trying to move it from sort of the conceptual realm to how do we operationally use that information and what space is PCORI in. It really has taken a couple of years to have that conversation and resulting really in this workshop with the experts.

That is conceptual work as opposed to these are actually work where we have done reviews, deliberation, contacted experts, went through a similar process as we did for the original set of standards.

These two standards were selected because this was an area where PCORI was doing a lot of work, and the standards could be helpful.

MS. HOLE-MARSHALL: Okay. Thank you.

DR. LAWRENCE: I just want to add to that. The decision sciences was meant to inform potentially funding methods portfolio or project

portfolio, because a lot of funding was going into decision aid. It isn't aimed towards standards. It's aimed toward informing PCORI about its activities in this area, which were already quite substantial.

DR. NEWHOUSE: The next set of standards are complex intervention. Brian, are you on the line?

DR. MITTMAN: I am. Thanks for the opportunity to present briefly from the West Coast. The process for developing standards for complex interventions, another set of new standards, follows basically the same process with a little bit of a twist.

First of all, examples of complex interventions include multi-level interventions that target health systems and health behaviors. Examples include public health campaigns that involves multiple components with multiple targeted audiences, also quality improvement or implementation strategies that involve multiple components in an attempt to change health system

policies or staffing arrangements, clinician and staff knowledge and attitudes, and other targets.

It is a different class of interventions. There is incomplete consensus as to what we mean or what is meant by "complex interventions." The first part of our process is actually to define complex interventions, to identify their key distinguishing features, and also to make some decisions about the scope of the standards, what types of interventions we view as complex versus simple, and which types of interventions and research questions will be addressed by our standards.

I won't take the time to convey details of what we are reading and discussing other than to say that this isn't a dichotomy, instead is a continuum from simple to complex. Most interventions have at least some elements of complexity, and that has been part of the complexity of this process.

Our next step after defining the scope and what we mean by "complex interventions," is to work

through a process of determining and discussing the key challenges in evaluating complex interventions. What makes them different from drugs and devices and other simple interventions that would warrant different standards, dealing with issues of the heterogeneity, variability and adaptability of these kinds of interventions, as well as the targeted individuals and audiences, organizations, that are addressed by those interventions.

Once we understood the challenges, then we moved into what is our standard process, identifying existing guidance to standards from published literature and from experts. Our first opportunity to obtain input from experts is listed on the slide, a half-day summit that is planned for the tail end of the PCORI meeting next week that will involve a set of individuals giving brief presentations and splitting into small working groups to identify challenges in the standards and guidance.

There will also be another meeting in December that is planned by Academy Health that we

will participate in.

That is in a nutshell where we are. We are in the midst of a literature review, and again, these upcoming meetings. Look forward to sharing drafts of our work later on this year and into next year.

DR. NEWHOUSE: Thank you, Brian. The last topic related to standards review relates to our review of the current standards that are in use. Of the 11 categories, the Methodology Committee with the help of the PCORI staff, has reviewed all of the methodology standards, learning from what we have learned internally from the funded PCORI proposals, from the PCORI staff with the Methodology Committee.

A Methodology Committee member was the link to each one of the standards. They have all been reviewed at least once on the Methodology Committee calls. We have one more to complete. Our plan is to review those changes for hopefully approval on the 29th. We hope to have that last standard ready as well.

MS. HOLE-MARSHALL: Robin, are these major changes? Can you just give us a preview? Are they substantially on track?

DR. NEWHOUSE: They are. I think that is what I would say. Many of them were questions about interpretation of words. It was really to add clarity. Others were organization. Others were some duplication between standards actually, to try to reduce any confusion or redundancy.

There were a couple of areas that required more deliberation, although at the end of the day, I can't speak for the Committee right now, but I think we have those revisions pretty ready to go without a lot of controversy or dialogue.

We will begin our review and vote next week to get ready for the 29th. Steve, wouldn't you say most were not substantive, they were really to add clarity based on what we have heard from the field and what we have heard from those that have applied to PCORI, or the people that have received PCORI grants.

UNIDENTIFIED: Thanks, Robin. I just have

a quick question about process. They don't need to have any further oversight, the MC approves?

DR. NEWHOUSE: We will actually bring them back to you in December like we did before for your review, before they are publicly posted. You will approve public posting if you think they are ready. After they are publicly posted, last time we received over 1,000 comments, I don't know what will happen this time but we will need some time to review each one of those comments and make a determination if changes need to be made.

We were very careful about those reviews. Then we will bring them back to you. I have a hard time estimating. I probably would under estimate that things will go very well and we won't have a lot of comments. By early next year, we should be bringing you back those final standards.

DR. WEISMAN: Robin, this is Harlan. Do you foresee after this review process goes through that a new version of the methodology report will be issued, standards will be issued in in total, including designs using clusters? That is part

one.

Part two, since I know you are going to be talking about dissemination efforts, are there any changes in the current standards that would affect the dissemination efforts of the current standards in terms of training and curricula?

DR. NEWHOUSE: I would say no at this point. Our goal was to provide some clarity in the language that was used, so a lot of it is definition and trying to make it much clearer for people to use. I don't think it will impact the training.

I do think the standards will be published quickly after approved, number one, and communicated. There will have to be some communication about the new standard, designs with clusters, but I don't think it will affect the dissemination efforts for CE or the academic curricula.

[Teleconference dropped for several minutes due to a PCORI technical issue.]

DR. NEWHOUSE: Technology is our friend,

in most cases. Yes, like over and over again. So, I think something that the Methodology Committee realized very quickly when PCORnet formed where there are many opportunities to partner with them to identify areas where there were additional methods, development. So she, Sally, stepped up very quickly to identify areas around data quality and missing data. So, she's been working with PCORnet at this point with an agenda drafted for meeting in December and data quality and missing data and patient centered outcomes research using EMR claims data.

So, this is one of those iterative kinds of exercises between the MC and PCORnet. She and Sebastian have been both leaders in that area to try to identified additional areas where we can be helpful.

So with that I'm thank you for your attention and wonderful questions during the presentation and also I would like to give credit to the Methodology Committee members PCORI staff members we work with. Thank you.

CHAIRMAN NORQUIST: Robin and Steve, by the way thank you again for agreeing to serve as the chair advisers -- you may not have known in your transit you were put back in. Thank you for agreeing. But anyway thanks so much to the methodology committee and what you guys are doing and what they're doing too. We really appreciate it. I know it's a lot of hard work. All right.

[Applause.]

CHAIRMAN NORQUIST: So at this point we'll move onto the next, unless Robin or Steve you had anything else you wanted to say at this point. Lori and Laura have now shown up. We were looking for you earlier I think, but now we've got you. So they're going to present an evaluation update -- results of the applicant -- Lori, are you going to go first or Laura? Lori, okay.

DR. SELBY: And as they take their seats and get ready, I just want to say again, that this work really came out of the last board meeting where members began noticing where we repeatedly fell short of the funding -- being able to

recommend funding to the extent we had secured your approval to fund. And Lori and Laura and evaluation analysis team teamed with -- particularly with three subcommittees of the SOC and you hear about the work from one of them today, work goes on in other fronts but I really want to thank them for their support of all of this work and as I always say the data keep getting better day by day. It always makes Lori cringe a little bit but I remember a year-plus ago Harlan Krumholz said something about, you know, you're a learning organization you need to get a handle on your own data. And I think we really have and it keeps getting better.

[Off microphone discussion.]

MS. FRANK: -- applicants in the applicant pool, but the first thing I'm going to do is turn this over to Laura, the Associate Director of Evaluation and Analysis and she can catch you up on what's been happening since last she and Diane Bild reported to you at the July board meeting.

MS. FORSYTHE: Thanks Lori. So in July we

gave you an introduction to the application enhancement workgroup. Our workgroup is made up of Rick Kuntz and Steve Lipstein and also Bob Zwolak as well as some other PCORI staff members. From Finance we have Hal Sox, we have other members from our Evaluation team including Lauren Fayish and as well as folks from our Engagement staff including Suzanne Schrandt and we work with a lot of other PCORI teams and departments.

And the group started developing a theoretical framework, that there are theories of necessary conditions for PCORI to receive excellent CER applications. You can see those here, they are important CER questions. That we have a pool of well-trained researchers, that those researchers perceive PCORI as a good fit for their work, and that we have policies that facilitate submissions.

And so, with that framework in mind the group has generated a number of hypotheses that might explain barriers for receiving the highest quality possible applications. And for each we systematically consider the hypothesis, we review

pertinent evidence, and consider proposed process improvement.

To-date we have presented you detailed information on three hypotheses. If you will recall at the July meeting we presented information from a variety of sources to demonstrate that applicants think the effort to apply is high relative to the likely of award, that applicants think timelines are compressed and that while researchers embrace the concept of engagement that they find our requirements to be challenging.

And so, the workgroup has reviewed a lot of evidence on these ideas and made some recommendations for improvements.

So outcomes of this work to-date include that we are doing a very detailed review of our entire application process. We're looking for opportunities to reduce the burden on our applicants, to streamline all of our processes and to increase the clarity and the consistency of all our messaging about our application requirements. And we want to take this opportunity to thank those

applicants that have already given us some feedback about our process. This includes through our regular applicant survey, after every cycle, but also some recent focus groups that we did with applicants and their feedback gives us ideas for our process improvements and also informs our strategy for this more detailed review.

The next thing that we've done is already extend the preparation time for applicants by introducing the concept of pre-award announcement. When topics are approved by the Board, like today, we want to start getting out as soon as possible as much information about the coming opportunity ahead of the formal PSA. And this is so that investigators can start thinking through their ideas and getting together the right teams so that they are ready to go when the PFA is put out. We're also considering other possible changes so that we can continue to increase the preparation time.

PCORI is also developing some ways to shift responsibility for some elements of

engagement; particularly ahead of the awards being made during the application process from the applicants to PCORI. And we're doing things like enhancing the engagement rubric and other resources about engagement.

MS. FRANK: Thanks Laura. So today we have three questions we want to address. The first begins with the description of the PCORI applicant pool. We're asking the question, do funded applicants differ from unfunded applicants along these dimensions in terms of their training, their years of research experience, and in terms of their history of interaction with PCORI.

The second question is whether there is a poll of well-qualified CER researchers out there who are not applying to PCORI and if so, why aren't they applying?

And the third question is about what proportion of health services and outcomes researchers might have experience with CER and/or pragmatic studies. So part of this is looking for the potential applicant pool for PCORI and what can

we learn from that in terms of increasing the size of the PCORI applicant pool.

So as you know we're collecting a lot of information around PCORI to be a learning organization and that the information that will bring to bear on today's questions are highlighted with those top three bullet points. We've conducted an analysis of applicant characteristics. We've conducted some literature searches with the focus of CER researchers to understand the potential applicant pool and we'll also share some data out of the researchers survey from our stakeholder survey work that you've heard some of.

And let's turn to the findings then. So addressing this first question. Do funded applicants differ from unfunded applicants along any of these dimensions and if so, what can we learn in terms of the PCORI application process about that?

So first I'd like to say that nearly every PI applicant PCORI has some form of doctoral degree and there are no differences by whether they are a

funded applicant, that's the awardee column there, or an unfunded applicant. There aren't any differences either by their proportions that have some form of a clinical degree. A little over half of all PCORI applicants have a clinical degree.

Where we do see differences is in terms of prior funding. So NIH funding, the majority of PCORI applicants have had NIH funding, but you can see proportionally more of the funded applicants relative to the unfunded applicants had NIH funding and proportionately more funding applicants than unfunded applicants had AHRQ funding, but fewer than half of all applicants.

We also asked about prior PCORI funding. PCORI funding is relatively new compared to these other institutions and there may be a little signal there, but those numbers are quite small.

Here we're showing funded versus unfunded applicants with funded applicants shown on the blue bars and unfunded applicants on the red bars. So here we ask them about their prior grant history in terms of prior grants. So looking for whether

there are differences by funding status, one way to break this up is to look at those left two sets of bars. So five or fewer grants.

The funded applicants, there were 32 percent in the five or fewer grant category. For the unfunded applicants it's 45 percent. Those proportions switch when you look at the upper two categories, I'm sorry, upper three. So if it's 11 or more prior grants.

This was any grant history, right. So the bottom shows you the end and information about our sample. So this really is just from the broad proposals for the funding cycles from August 2013 through Fall 2014.

So, those numbers flip on the upper end. So it's 42 percent with 11 or more grants are the funded awardees to PCORI versus 31 percent of unfunded. We are really glad to see individuals with no prior grant experience applying to PCORI.

We also asked about this size of the prior grant. So here you can see we have funded applicants in blue and unfunded in red. There's a

trend for funded applicants to have had larger prior grants than unfunded applicants.

A point I'd like to make here, too, is we had a lot of questions about very experienced researchers. So those all of the way to the right they're those who had a prior grant of $10 million or more. We looked at the set who also had 21 or more grants. So this is a very experienced set. Because one of the hypothesis was that perhaps these folks are the unfunded among them are doing very well on technical merit but not doing as well on PCORI unique criteria like patient-centeredness and patient-engagement, but in fact data don't support that hypothesis. The profile of merit review scores for that very experienced set of researchers is similar to that for any unfunded applicant.

Another question we had was how experienced are PCORI applicants? So you can see the majority have 10 or more years of research experience, no differences between the funded and the unfunded applicants here.

Once again, I want to say we are pleased to see relatively junior investigators applying to PCORI and with some success.

And then here, finally, to address this one question we had asked applicants about their prior experience interacting with PCORI. So we divided their prior experience into high intensity, medium intensity, and low intensity. High intensity prior experience means things like serving as a merit reviewer or participating at an in-person PCORI meeting or interacting with a PCORI staff member. Low intensity are much more passive forms of interaction like receiving notices from our listserv or going to our website. That medium level then is somewhere in-between, so accessing PCORI materials online like training.

And so, you can see that a higher proportion of the funded applicants had high intensity prior interaction with PCORI than unfunded applicants.

So, from this data we concluded that PCORI applicants are generally experienced researchers

with demonstrated success at other funders. Training doesn't differ between funded and unfunded applicants, but more funded PCORI applicants than unfunded applicants do have a history of funding from NIH or AHRQ. And about 70 percent of funded applicants reported high levels of interaction with PCORI, only about half of unfunded applicants reported this high intensity interaction with PCORI.

So, let's turn to the second questionnaire. Is there a pool of well-qualified --

CHAIRMAN NORQUIST: Wait, wait. Let's just see if there are any questions --

MS. FRANK: Sure. On that set.

CHAIRMAN NORQUIST: Let's go to that one if anybody wants to -- yeah, Rick Kronick.

MR. KRONICK: Yeah, would you go back one slide please. You know, as I saw your results which I think are very interesting and useful. I'm not sure I come to quite the same conclusion as your first bullet. It's certainly experienced and successful researchers are more likely to be

successful with PCORI than less experienced folks and that kind of makes sense for all kinds of reasons.

But it also seems like you had quite a few folks who are no so experienced. I mean, at least 30 to 40 percent through what you count there.

MS. FRANK: Yeah, so on this first bullet we're limiting it to a description of applicants generally without getting into who was successful. So you're absolutely right with regard to application success. But one of the first questions we had was to what extent is PCORI attracting seasoned researchers?

MR. KRONICK: It seems like seasoned researchers are applying as are somewhat junior folks as well.

UNIDENTIFIED: [Off microphone.]

CHAIRMAN NORQUIST: Yeah. Alicia.

DR. FERNANDEZ: I found this really interesting and I have two questions. One is if you've had a chance to look at generalists versus specialists for the clinical degreed researchers.

And the other one had to do with -- I was very surprised with the large number of people and I wanted to make sure I understood it correctly who don't have a clinical degree. Meaning they are PhDs for example, a PhD epidemiologist or something.

MS. FRANK: Exactly.

DR. FERNANDEZ: And I was wondering whether you had looked to see if that's all being -- you may not have had a chance to delve deeper into that, but if you could say anything more about that that would be interesting.

MS. FRANK: Sure. So first I'll say we take requests, so we are very interested in hearing your questions. As Joe mentioned we're accumulating more and more data. We have a lot more from which we can ask questions. In this case we have not yet looked by specialist versus generalist, but you're absolutely right that a little less than half of PCORI applicants have a doctoral degree in something other than a clinical field.

CHAIRMAN NORQUIST: Steve Goodman.

DR. GOODMAN: How likely in particular unfunded applicants are to reapply? Not the same applications that apply again in the future.

MS. FRANK: So we're looking at resubmission data now. We don't have don't have those to share fully yet. We do have, as you know our applicant survey we ask after each round, so the question is do we ask them specifically about whether they intend to reapply and I'm looking to Laura who would have the answer.

MS. FORSYTHE: I believe we do ask them how likely they are to apply again in the future and that's something we can report back to on. And in addition to our analyses looking at what proportion of applications come back to us as a resubmission, we're also looking at more detail in terms of what portion of applicants come back to us with something else. Whether it be an LOI or full application, to understand the full trajectory particularly now that we have a competitive LOI process to figure out who is coming to us with how

many submissions and how successful they are over time.

DR. GOODMAN: I guess what I'm trying to get at and I'll be very interested to see those data, is one of the ways people choose where to submit their funding is basically through word of mouth, recommendation on the street by fellow researchers and if there is the word out that -- it's just like journals as well, that PCORI is thought unfair, capricious or generous, quick and helpful, you know that's just not the perception that's held by a particular researcher but could spread to their entire division or team or institution.

So, the more you can get a handle on that and I don't know to what extent you have, the better, because it is that reputation on the street that profoundly affects where people will send their first application to.

MS. FRANK: Okay, terrific. I'm wondering if there are any other questions because that would be a great segue.

CHAIRMAN NORQUIST: So, questions?

MS. GOERTZ: Can you -- sorry I missed it. Is this a survey data or are you pulling this from their applications?

MS. FRANK: So we ask the applicants to self-report on a number of different pieces of information about themselves, so that's where we're pulling these data.

MS. GOERTZ: As part of the application process?

MS. FRANK: Yes.

MS. GOERTZ: Do you have information on how long it's been since they graduated with either their clinical degree or their PhD?

MS. FRANK: We do have information on seniority that way, not for all cycles. So we'll put that on our list to get back to you on. Is there a hypothesis specifically on --

MS. GOERTZ: Well, I'm just curious about whether people that are successful tend to be people that have been -- you know, in the field for a really long time or more people who are really

just getting started in their careers. You can draw some conclusions form how many grants they've gotten, et cetera, I think but not necessarily answer that question directly.

MS. FRANK: Yes, so we did ask them about their self-reported number of years of research experience and that's where we saw the vast majority -- about 75 percent of applicants had reported 10 or more years of research experience specifically.

MS. GOERTZ: Thanks.

CHAIRMAN NORQUIST: So on your self-report survey, is that a 100 percent response?

MS. FORSYTHE: Right. It's questions applicants answer at the time of submitting their application.

CHAIRMAN NORQUIST: So it's 100 percent.

MS. FORSYTHE: It's part of the application process.

CHAIRMAN NORQUIST: Okay. All right. So your second point.

MS. FRANK: Okay, so to Steve's point.

Yeah, we're all very interested in knowing what's the word out there about PCORI as a potential funder. Absolutely.

And so, one of the ways we're addressing that question is here. We're wondering what's the potential applicant pool, who is applying? If there are people who aren't applying, why aren't they? Is it because they're not aware of PCORI? Or have they heard about PCORI and they choose not to apply to PCORI for funding? We really want to know the answer to these questions.

So there's a couple of different ways we're going about answering this. I'm going to show you some information out of some literature searches. This work is led by Michele Orza with assistance from Lauri Davidson, our Medical Librarian, Nick Wilson and many, many others.

So here is one search. It's a year's worth of published literature, April 2014 to April 2015. Looking for CER as identified by the authors or by National Library of Medicine indexers, and you can see our search terms there. We're really

looking for CER. We also had search terms in there for study design and this was because we were looking for empirical studies. We didn't want articles about CER; limited to the English language.

So the yield for this was 216 articles. We were interested to see how many were conducted outside the U.S., we set those aside for now and wanted to focus on the remaining 136 that were conducted in the U.S.

Of those, how many of those authors are connected to PCORI in some way. And so, the short answer is 55 percent have some connection to PCORI. So, the connection is about 30 percent of them actually have PCORI funding, another 55 percent have applied for PCORI funding.

Another way the team has gone about answering this question is to do a more focused search. So here the focus is on CER trials specifically. Looking at these five top journals. Looking at less time, so not a full year's worth.

DR. SELBY: Lori just emphasize that the

search strategy here was different. So this is not a subset of the earlier presentation.

MS. FRANK: That's right.

DR. SELBY: If you could say anything about search strategy at this time.

MS. FRANK: Yeah, so here the goal was to collect information on published authors who had clearly labeled their work as CER. So this was a completely different effort than that first search. In the background, this team has been running multiple other literature searches. So we're just showing you some of the ways in which we were =trying to identify the pool of potential PCORI applicants and understand first of all, PCORI's reach with that potential applicant pool. But then, we're following up with the folks.

DR. SELBY: One point. This is a group that may not even quite appreciate sometimes that they're doing CER because they didn't have say the word CER to get into the sample. Because they said versus, that was actually one of the better traps.

MS. FRANK: Right. So most of these

studies, in fact, Michele has found aren't clearly labeled as CER as Joe said.

So this search yielded 141 discreet studies and even higher proportion of those were conducted outside of the U.S. So again, we were just focusing for now on U.S.-based studies; a very high proportion are connected to PCORI in some way. This includes, for this, it's actually the first, second, third more senior author.

So that note there, we're collecting feedback from a subset of these. So we reached out then to that minority who aren't connected to PCORI in some way and sent them an e-mail saying we would love to follow up with you. We would love to hear from you. And so far we've been on the phone with about 10 of these researchers who've taken us up on the offer to speak with them by phone and we've collected a lot of other feedback via e-mail.

And so, very preliminary themes sort of haven't emerged from those conversations, but I can show you on the top left there is something that we hear from other corners as well that there's an

opportunity cost in switching set, essentially, from a known funder to a new funder. In the upper right is a set of themes -- this is representative of the set of themes we hear about people preparing to apply to PCORI for funding. They say, "I know you're out there. I want to apply. I think my research is getting ready, but it's not quite there yet and I'm working towards the PCORI application." So that's a different group.

The bottom two quotes are similar themes coming from researchers who are a bit stymied about how to engage research partners in observational studies or secondary data analyses and even lack of clarity about whether PCORI will fund secondary data analyses.

So conclusions on this line of inquiries. We've found that PCORI is in fact reaching a high proportion of U.S.-based CER researchers. Certainly there is more work we will do in terms of outreach to this potential applicant pool to make sure we clarify PCORI's funding requirements.

As a result of this, we actually added a

question then to the survey that we give to our merit reviewers after each round of merit review. We ask if you have applied to PCORI and if not, why not? And we hope to report back to you on that fairly soon.

So now I'll turn it over to Laura.

CHAIRMAN NORQUIST: Wait. Let's see if there are any questions about this.

DR. GOODMAN: Just one really quick question. I'm interested you didn't search for the term patient-centered outcomes research. Why? Maybe that's clearly not a standard, but did you include it at all?

MS. FRANK: So, Michele could probably speak to this better than I can and you're welcome to reply Michele, but the first question was among published CER researchers, what do they know about PCORI and why aren't they applying? Because we are looking for people with strong CER expertise primarily. Do you want to add to that Michele?

MS. ORZA: [Off microphone.]

CHAIRMAN NORQUIST: We can't hear you

unless you speak into the microphone. The people on the phone can't hear you.

MS. ORZA: So we've been experimenting with a couple of dozen different kinds of search strategies to see what gets us what we want. And we are working on trying to identify PCOR specifically, but we are not able to show you that today.

DR. GOODMAN: This is great work, this is really interesting. I'm shocked how high some of those numbers are. Especially so recently. I thought you were going to find it was low because these were applications on work that started many years before, so really, really very interesting.

DR. SELBY: You're surprised at what a high proportion are connected to PCORI?

DR. GOODMAN: Yeah.

CHAIRMAN NORQUIST: But then the issue -- it is surprising, but are we funding the same -- where are the new people? But anyways.

UNIDENTIFIED: I'm also surprised how small the denominator number is. I expected that

to be bigger.

CHAIRMAN NORQUIST: Yeah.

MS. GOERTZ: I wonder if there is some value also looking at the people who weren't first, second, third or senior authors because those folks in the middle, I think, would be really one of the audiences I would be interested in targeting.

CHAIRMAN NORQUIST: You're pointing at somebody?

MS. ORZA: Sorry. So in the first set we looked at the first and last author of every study and the second set we looked at the first, second, third, and last and we're trying to identify specifically the PI and following up with them.

MS. FRANK: But to your point, absolutely. If we're looking for the potential market of PCORI applicants, there it is in the whole author set. We agree. So we'll get back to you on that.

CHAIRMAN NORQUIST: Okay, so number 3.

MS. FORSYTHE: Okay, so our third set of questions are what proportion of health services and outcomes researchers have experience with CER

and with pragmatic studies and what proportion could be PCORI applicants and what should be done to increase that.

So to answer those questions we turn again to our PCORI survey or researchers. You first heard about this effort in more detail at the January board meeting and we fielded this survey in late 2014 to clinical, health services, and health outcomes researchers that we invited via 23 professional organizations as well as the PCORI mailing list. We heard back from 508 researchers. they told us they were pretty familiar with PCORI. In fact, 59 percent of them had applied to PCORI and 43 percent of those had received PCORI funding.

So it's really important to note that this is a PCORI savvy group and that has some important implications for our interpretation of our findings, particularly related to experience conducting CER.

So of those researchers, two-thirds indicated that they had conducted CER before and of those, three-quarters, said they had done

observational studies. About two-thirds said they had done secondary data analyses. Just over half said they had done randomized trials. And just over a quarter said they have done pragmatic studies.

And that information is relevant for PCORI as we think about what kind of studies we want to fund going forward, particularly large pragmatic studies.

And we asked this question in part to try to better understand the array of CER research interests and to consider what kinds of work people are doing, because some are relevant to the kinds of CER that PCORI funds and some of them are not.

So in conclusion among these researchers we heard from health services and health outcomes researchers that they have more commonly conducted observational studies and secondary data analyses. And they have used other methods; about half said they've done randomized trials and about a quarter reported experience with pragmatic trials.

Also, I want to remind you that at our

July meeting we talked about how researchers have told us that they like the idea of engagement but they find that challenging. And with that in mind, that may further narrow the pool of CER researchers, particularly that are prepared to do patient-centered CER with engaged approaches to doing that work. And so, that may present some opportunities for PCORI to increase our support, our training, and our outreach to potential CER researchers.

MS. FRANK: Okay, so any questions on what Laura just presented?

CHAIRMAN NORQUIST: Questions about that? Christine.

MS. GOERTZ: Thank you. Do you have any idea at all what the denominator is for that because it seems to me that who is going to respond are those people that have an interest or know about PCORI, so I'm just wondering if we have any sense of what the denominator is.

MS. FRANK: So for that we don't. We have a ballpark sense because we know what organizations

we went to and what their membership size was. but yes, the folks who responded to that survey are those health services researchers who are obviously very PCORI savvy.

MS. GOERTZ: What is the ballpark? Are we talking thousands?

MS. FRANK: Thousands, yes.

MS. GOERTZ: Okay.

CHAIRMAN NORQUIST: Okay.

MS. FRANK: Okay, so from all of these lines of evidence then we have some conclusions. The pool of health researchers who are successful with other funders is large but as Laura said, that narrows when you're looking at that set of researchers who can conduct randomized trials and/or large pragmatic studies. And we were interested to see differences between funded and unfunded applicants in terms of their prior interaction with PCORI. There's potential opportunity there for outreach and continued interaction with potential applicants.

And one way we think PCORI can expand the

pool of eligible researchers who can be successful applying to PCORI is to not only continue with the outreach and informing the research community about PCORI's application requirements and the opportunity that it offers, but also as Laura said to support the community to become more capable in patient-centered research and engaged research.

So, we started with some action items from the last time. As we accumulate evidence, we turn it into action as much as possible. So we're using input from prior applicants to improve the process. We're undertaking an analysis of resubmissions and look forward to reporting to you on that. We are tracking the proportion of CER researchers who are applying to PCORI to monitor ongoing outreach efforts and we do intend to continue to ask those who are not applying, who we think are in the potential PCORI applicant pool, why not?

And then, on that last point there, the merit review. We think that we're interested in understanding more about the relative strengths and weaknesses of the critiques for funded and unfunded

applications. There's something there that we can learn in terms of guiding applicants and there's something there in terms of improving our own internal processes.

We welcome any other questions.

CHAIRMAN NORQUIST: Any other questions, recommendation to them? Rick.

DR. KRONICK: This is really useful. A couple of other potential pools of folks to look at might be former AHRQ grantees when we used to fund comparative clinical effectiveness research.

My suspicion is a very, very high proportion of those people are involved with PCORI, but then a second pool with maybe a lower penetration rate from PCORI would be folks who are NIH grantees who are doing CER. And again, I know you've been reviewing the published literature, which certainly makes sense, you know, and is probably the best approach but if you're also trying to see what does that pool look like there are probably some folks who are relatively new researchers who've gotten grants from NIH in CER

that would have yet to show up. And I can imagine, may be fewer of them have experience with PCORI and they might be a group to go after.

MS. FRANK: That's a great suggestion. Thank you.

CHAIRMAN NORQUIST: Yeah, I know, for example, some of the institutes have funded traditionally more CER like the National Institute of Mental Health, and as they started to shut that down I've watched those people, they've come over here or tried.

Alicia.

DR. FERNANDEZ: That was really interesting. This may be premature, but I was wondering if you or perhaps Joe or Rick could tell us a little bit about does PCORI have any thoughts about training opportunities for young researchers in CER and any -- I don't know what discussions have gone on about that and to what extent they're relevant to bring up at this point and certainly how that would differ from AHRQ.

CHAIRMAN NORQUIST: You know, that's a

good point. Let's see what Rick --

DR. KRONICK: Do AHRQ has awarded a series of institutional training grants and a variety of other K awards in training. We're also working on -- and in conversation with Joe and PCORI folks -- on trying to figure out what are the training needs, particularly for learning health systems. So a little bit different than, I think, the folks that Lori is focusing on here.

So the awards that we have made are very much with the goal of providing support and training researchers who would be applying to PCORI for money. We are, as I said, working on trying to figure out what are the training needs for researchers who are going to be working in health care systems and those are, I think, different -- that's a work still in progress.

DR. SELBY: And I'll just add, this topic is under active consideration by the RTC and you'll be -- I suspect, hearing a report from the RTC is two to three months. but we've had Bob Kaplan from AHRQ join the meeting. We're pretty impressed with

the portfolio of training opportunities that AHRQ already has in place and the number of awards and funding levels.

But originally coming out of the meeting we held with PCORnet systems leaders a year ago at the IOM, this notion of training people who really would be embedded in health care delivery system, to ask and answer questions with the researcher's rigor on a timeline and with the outcomes in mind that mattered to systems is an area that nobody's really ever funded. We talk learning health system, but we don't talk about preparing a workforce for it.

So that's a strong mutual interest. I'd say the RTC and I don't know if Freda is still on the line, but it's --

DR. LEWIS-HALL: I'm here.

DR. SELBY: Freda, if you want to add anything go right ahead.

DR. LEWIS-HALL: Nope, you're rocking and rolling.

DR. FERNANDEZ: Can I make a comment then?

CHAIRMAN NORQUIST: Yes.

DR. FERNANDEZ: Freda, I think it would be in maybe our all-over list, but I think it would be really interesting when you all come forward to have a broader discussion. I would be very interested whether you considered different forms of grant mechanisms within PCORI more similar to R21s or smaller mechanisms that would let people get their feet wet in comparative effectiveness research, particularly in patient-centered research in that sense, before they're ready for something that would be in our broad -- in other words to think of PCORI's role beyond funding or helping to fund traditional training programs, but also how we might change our portfolio to bring forth a more -- to help train young researchers.

DR. SELBY: I think that's a great suggestion. I really do think these data are very interesting. Somehow I think I still have this pretty strong conviction there's a group of people who we will call clinical researchers out there. Some of them were in the 35 to 45 percent who

hadn't every heard of PCORI, but people who were just not yet ready to move from a sort of an explanatory clinical trial to a more pragmatic clinical trial. Those programs that would be toe-dipping exercises for them would be a good idea.

DR. LEWIS-HALL: I also think there's an opportunity for us to leverage people from -- if you would, from the other end. People who are not clinical researchers. I'm doing air quotation marks -- "per se," but who have a keen clinical interest in some very important questions and could be brought into the fold with a new perspective if we gave them exposure to this new way of getting research done.

I think we can do it from all angles, beginning to draw people in from various places in the clinical/investigator ecosystem to become a part of this and that's why I think that training programs that are atypical in many ways are an important consideration and toe-dipping is a really important part of that.

DR. SELBY: I failed to mention too,

Harlan Weisman, who I think is on the call is actually leading that work, so Harlan if you're still on -- for the RTC, if you're still on please jump in.

DR. WEISMAN: Thank you Joe and I am still on. I don't think I have anything to add to what you said. I'm really excited about the possibility of working with AHRQ on addressing, you know, this training need and then presenting to the Board as we start fleshing out the details of what it might look like.

CHAIRMAN NORQUIST: So we'll let Bob Zwolak -- you get the last comment.

DR. ZWOLAK: Thanks very much. I wanted to, as the chair of this workgroup on behalf of Rick and Steve Lipstein, I wanted to thank Laura and Lori and Michele for these superb analyses. I was struck by a number of things.

I was very much struck by the penetration of PCORI research among established investigators. I was struck by this seemingly low number of investigators who actually are skilled or admit

skill and performance of RTCs in advanced pragmatic trials and certainly the opportunity for education has been well-addressed here.

We started out trying to figure why there was a relatively low number of high quality applications and how we could enhance it, and I do think we've made some substantial progress. So thanks very much for your help.

CHAIRMAN NORQUIST: Yes, thank you both. So as Rachael Fleurence and Joe, you're up now too. The last session before our public comment is on the PCORnet Phase II, so Freda we need you to stay on too. Rachael, come up to the front here.

DR. SELBY: I think Rachael is going to make the presentation. I'm going to be here for questions.

CHAIRMAN NORQUIST: Okay.

DR. SELBY: She will do her usual competent job.

DR. FLEURENCE: Good afternoon. I am going to do the PCORnet Phase II presentation update. We have a lot of different work streams

from PCORnet right now, so I'm going to try to sort of wrap it all together nicely for you, but there are a lot of sort of disparate work streams that I'm going to be presenting.

Phase II networks are on board, so I'm going to give you a little bit of information about who they are. I'm going to talk to you about the PCORnet demonstration projects and initiatives, a little update on the PCORnet common data model, which is the data model that allows us to do a lot of the analysis ready work. I'm going to talk to you about progress from PCORnet governance, and the new governance structure that was approved at the end of August by the PCORnet Council.

I will give you a brief update on the PCORnet business plan which had been a request from the Board back in February and we now have some draft recommendations to share with you.

Then we have some time for discussion.

Starting off with a few words about the Phase II networks, on July 21, the Board of Governors approved the Phase II networks. We now

have a total of 33 networks including both CDRNs and PPRNs. There are 6 new networks within that number, four are PPRNs. I'm going to go through them very briefly for you.

The first new CDRN is called LHSnet. It is based out of Mayo Clinic, although it does cover 10 million patients across the country, and most interestingly I think for PCORnet, it has three million patients with linked claims and claims in the HR data.

The second CDRN is OneFlorida. It is run out of the University of Florida. It also covers 10 million patients across the State of Florida and also has a lot of integrated claims in the HR data already conducted.

On the PPRN front, we have an Interactive Autism Network led by a patient care giver, Jessica Law, also connected with Johns Hopkins. We have a PRIDEnet PPRN, this is a disease diagnostic PPRN that is concentrated on sexual and gender minorities.

We have an Alzheimer's and Dementia

Patient and Caregiver Network, out of Mayo Clinic, and co-led by a caregiver. Our fourth new PPRN is a Community and Patient-Partnered Participatory Research Network (CPPRN). This is focused on behavioral health in under resourced communities.

That is sort of the broad overview of our new networks and as we slip into Phase II, we are right in the middle of contracting right now, and are looking at a fairly seamless transition from Phase I to Phase II, which will be three years.

A few words now about the demonstration projects. First, our clinical trial, ADAPTABLE, which compares two different dosages of aspirin. This is the first pragmatic clinical trial for PCORnet. The protocol has gone through a number of reviews with our CTAP Subcommittee as required by the PCORI process. Recruitment is scheduled to begin in January 2016.

The second set of demonstration projects are the observational studies around obesity. They were both approved in August by the Board. One is on CER of bariatric surgery and the second one is

on looking at alternative antibiotic regimens in a pediatric population. Again, the CTAP Subcommittee is providing recommendations around these protocols as we finalize these and move to contracting.

The PPRNs, you will recall, also have some demonstration projects. The first set are well underway. We have letters of intent that were received and approved and full applications are due actually on October 14, so in two weeks. A little further down the pipe is the cross-PPRN demonstration project, and its release is anticipated for the next month, so fall of 2015.

A few words about the Natural Experiments Network. This is a collaboration between PCORI, the CDC, and NIH. PCORI will be funding up to three projects under this research network. It is focused on diabetes. The CDC and NIH have made their decisions about their set of fundees. Two of them are CDRNs, so we are excited to be able to announce that today, and PCORI will now be reviewing additional applications in order to fund up to three of these networks under this Natural

Experiments Network.

The Health Systems Demonstration Projects, building on our prior work where we engaged with the IOM. We have provided supplemental funding to all the CDRNs to work with their health system leaders. Over the next few months, the CDRNs will be working with these leaders, to engage with them to discuss potential topics, and in January, the National Academy of Medicine will host a follow up meeting with the CDRN leaders. We will then award up to five one year studies through a limited competition and we expect that to be posted in the spring of 2016.

Another critical initiative that will be coming out of PCORnet is a collaboration with health plans. I talked before with the Board about how critical it is to have these relationships in place with the health plans in order to link the CDRN and HR data with claims data. We expect to fund up to two major U.S. health plans in this area, and the PFA is scheduled to come out within the next month, very close to being finalized. We

hope to get that work underway very soon.

Moving on to sort of after the demonstration projects, just a quick update. We wanted to show you where the common data model of PCORnet is right now. You don't need to read all of these tables.

The main point that I wanted to make for today is we are on Version 3.0, so within 18 months, I think we are fairly happy with the progress there. Common Data Model 3.0 is also built so it can respond to the clinical trial needs of ADAPTABLE, so we will be using the Common Data Model for the clinical trials.

Currently, there is about 62 million patients who have data transformed into the Common Data Model of PCORnet. There is still quite a bit of work to do around quality and longitudinality of the data, but that gives you a sense of the scale of what PCORnet might be able to do with these 62 million patients within the Common Data Model across the 11 CDRNs. This does not account yet for the two new CDRN networks.

Moving now into governance and sort of generally operational work that's going on within PCORnet. We have a number of critical work groups formed early in the summer. This is just sort of giving you a highlight of what these work groups are focused on and what they will be delivering.

We have a Dashboard similar to the one PCORI uses for this Board of Governors. We are producing a Dashboard for PCORnet and its steering committee, now called the PCORnet Council.

We have a front door policy so where to knock on the door, how to knock on the door of PCORnet. That is currently under development and will be ready in October. We have two really critical work groups focused on IRB and contracting for PCORnet. These are really, I think, potentially transformational just as much as the data infrastructure piece. We have a lot of effort and energy going into sort of pushing these work groups forward.

We also have an engagement work group that continues to outline engagement strategy for

PCORnet, including both patients, but also importantly clinicians. Finally, we have an industry work group building on several outreach efforts that have already been made this past year that were led largely by Bryan Luce and Adrian Hernandez out of our Coordinating Center at Duke. These are the work groups that are really starting the business development work and the contacts with industry.

A few words about governance. PCORnet is evolving from a very sort of traditional structure where PCORI funds 29 individual networks and the coordinating center to something where the networks are more engaged with each other, and for that we needed a change or we needed a governance structure that supported that.

On August 31, PCORnet's steering committee, now called the PCORnet Council, voted to approve their governance, it is a six to eight page document that lays out decision making and lays out sort of different critical committees that will help run PCORnet, in addition to the Executive

Committee that has been functioning now for over a year and a half and functioning well. We are now adding an engagement, data, and research committee to PCORnet.

A few words in closing around the business plan development. Again, this was an ask of the Board back in February. We engaged with PriceWaterhouseCoopers in May to develop this business plan for PCORnet. They have done a huge amount of ground work and interviews and background work, interviews with key stakeholders. They also held an one day meeting with key stakeholders within PCORnet, and are in the final stages of putting together their recommendations to PCORI. These recommendations will be presented to you shortly. They first need to be vetted by our legal counsel and by the PCORnet Executive Committee to ensure they can be disseminated.

The bottom line of the business plan is they are recommending a contractual consortium model and have a number of supporting evidence and documents to support that recommendation.

That is the end of my presentation.

CHAIRMAN NORQUIST: Great. We will start with Barbara McNeil.

DR. McNEIL: I'm not sure I know what a "contractual consortium model" is.

DR. FLEURENCE: It's a model whereby each network has agreed to sort of link with each other through a participation agreement or contract.

CHAIRMAN NORQUIST: I'm sorry, there's some feedback on the phone.
Okay. I'm not sure who is on the phone but they may need to mute their phone.

UNIDENIFIED: My fault, Gray; sorry.

CHAIRMAN NORQUIST: Go ahead.

DR. FLEURENCE: The conversation about PCORnet sustainability is ongoing and it generally involves speaking of PCORnet being its own independent entity at some point down the road, sort of once PCORI funding goes away. The questions have been how would this entity be supported from a legal and structure point of view, and having a consortium is one of the proposals on

the table for it.

DR. McNEIL: Just to make sure I understand, there are lots of pieces on this, does that mean each part makes an agreement or contract with every single other one? I just don't understand the mechanics.

DR. FLEURENCE: There would be a participation agreement that would be central and it would link all the participating organizations that wanted to be part of the consortium, so we don't know that all of them would want to be, that would replace right now what we have, sort of the 29 individual contracts that link PCORI to each of the networks. That is really all that holds PCORnet together right now, these individual contracts. What we are looking is something that holds them together without going through PCORI.

DR. McNEIL: Does that mean, pretend there's A, B, C, D, E, whatever they are, they all go into a central something, does it mean A and B cannot get together without going through the central whatever you are calling it?

DR. FLEURENCE: It does not mean that. From a research perspective, networks will be able to get together potentially using resources that are now part of the PCORnet Common, so they will have data that has been standardized, they may be able to use the operational building blocks, streamlined contracting. It is not necessarily that they are all working through a central coordinating center or program office, but there has to be some sort of glue that holds them together. Right now the conversation is around what this glue is.

DR. SELBY: Rachael, I think we could say in the PWC, the PriceWaterhouseCoopers proposal, there is a recognition that something has to replace the centrality of PCORI in this. What it is is going to have to be worked out.

The Governance Committee has strengthened the Executive Committee of PCORnet, but this collaboration agreement is going to have to be signed by anyone who is a part and probably they are going to have to be signatures between each

network and some central function. That is going to take a bit more time to work out, exactly what that central function looks like.

For example, to the front door, to the place that receives a large proportion of the proposals for funding, one thing as Rachael said, it's very strongly held, participating members don't always have to go through that central function. There can be PCORnet studies that involve two or three networks that don't necessarily go through the central function.

CHAIRMAN NORQUIST: Alicia was next.

DR. KRUMHOLZ: I have a question as well.

DR. FERNANDEZ: I have two questions. Would you mind going back to the governance slide? I just wanted to be sure I understood the slide and whether or not there were non-investigators represented and how they were represented and the inclusion or not of other forms of non-investigators. I have another question.

DR. FLEURENCE: That's a great question. The PCORnet Council is our former steering

committee, so there's one PI per network. Our PIs are now, especially on the PCORI side, we do have a patient co-PI that was a requirement to come into Phase II, so some of our PIs are actually going to be patient co-PIs sitting on the PCORnet Council.

I guess they still have the title of investigator, but we expect to have a number of patient PIs or co-PIs sitting on the PCORnet Council.

Similarly, our committee chairs may or may not be researchers, but they may also be patient advocates or people representing patients.

I think we have done a lot of work to ensure and push sort of wider representation within PCORnet, similar to the work we have done at PCORI.

DR. FERNANDEZ: I think that's useful. Thank you. I guess my question may be this was already approved already or maybe it doesn't need to be approved by us or whatever. I don't know what the relationship is. I wonder whether we feel if this entity is definitely going to live on after PCORI or we are making plans for that perhaps, who

knows, whether we feel comfortable about the inclusion of stakeholders and the governance that has been set up or the governance model going forward. We may feel very comfortable with it.

I also don't know that I really understand our relationship, and perhaps Gray can comment on that or someone can comment on that later.

The second question I had was a more minor question but it's not completely unrelated, which is did I understand that we are going to fund two health plans to see whether or not they can link their data? If so, I'm curious, if I understood that correctly, about that role of incentivizing that particular linkage, if I understood correctly. Was that external to PCORnet?

DR. FLEURENCE: Yes, I think when the vision of PCORnet came out, the expectation was that the networks that would come in would be health plans working with delivery systems so we would have these linkages.

The reality of who came into PCORnet is its largely NEHR based systems. We do have some

integrated delivery systems, including Kaiser and Group Health, but largely this is NEHR based networks.

The funding is to work out the important governance issues and how this might be linked. I think where we are heading right now is sort of apply some of the use cases to our demonstration projects, potential linkages, particularly around the aspirin clinical trial where we would try out the relationships.

CHAIRMAN NORQUIST: I'm not sure we came to a conclusion. That's been something they have been working on. I think it's an issue, we should have some further discussion about representation. At some point, it's out of our hands, once they move onto something else, they can do it. I guess that's for further discussion, Rachael.

DR. FLEURENCE: Also, we have had really vigorous conversations at the PCORnet level around representation and patient representation. We had the PCORnet Patient Council for the first year of PCORnet's existence that had vigorous opinions

about representation, and I think we had really healthy back and forth with patient groups, with the patient PIs, with the PIs. That played out quite a bit over the summer as we came to this governance structure.

The potential particularly for patient representation on the PCORnet Council is very high, given that our 20 PPRNs have either patient PIs or co-PIs.

CHAIRMAN NORQUIST: One way to find it out is you could ask the people who are listed as the stakeholders if they feel like they are engaged. It would be interesting to see whether they feel they actually are represented.

DR. KRUMHOLZ: My observation at the meetings has been -- I haven't attended very many -- the Executive Committee, the patients are there. They don't have the same degree of voice as the academic investigators. On an ongoing basis, they need protection, if you will.

UNIDENTIFIED: Two comments and one question. The governance issues are clearly going

to be very complicated. They are very difficult. Alicia raises rightly the question about representation of patients.

A comment is this is going to be obviously very hard to make work, and I would encourage representation of people who know how to make a non-profit sort of small business work. The other side of this, as I think of PIs who are likely part of this now, this is probably not mostly in their skill set. It's a different skill set. I'm sure PWC talked about this.

The second comment or maybe a question, I know you have had discussions with CMS about trying to get Medicare and potentially Medicaid, much harder data in, but as you mentioned the potential contracts with health plans, I'm wondering where those stand, but then the real question is about the queries that were promised. I think the last time you presented, Phase II had some number, I forget if it was 50 or 100 queries that were supposed to coming out of PCORnet, and I wondered what the status of those are.

DR. FLEURENCE: On the CMS front, we do have a pilot that is led out of Duke, our coordinating center, working with CMS on the Medicaid data. That's a pilot that is underway. We are making progress on that front.

DR. SELBY: You said Medicaid, but I think you mean Medicare.

DR. FLEURENCE: Yes, Medicare. To your question on queries, we are getting very close. We don't yet have a nice clean process where the knock on the door is answered in a way that is transparent and open yet to everyone because we are still working out the final pieces. That is what the front door working group is working on.

As part of the contracts for Phase II, all our networks do have a certain number of built in queries, and I think it is 50 for the first year. We are very close. I think we have sort of flipped into Phase II as contractually required by our networks -- organized in terms of how these are going to be sent and who gets to ask. We are definitely much closer than in May.

CHAIRMAN NORQUIST: Bob Zwolak.

DR. ZWOLAK: Rachael, that's a huge amount of work, congratulations. My question has to do with the fact that we are building this research blockage and right now, PCORI, I think, is buying some fuel with the aspirin study and the bariatric study. What other customers are there out there who want to use PCORnet, and do you have any hard commitments for monies to fund research trials through PCORnet or at least any promises? Are you building an one pager like Lew Sandy said for PCORI itself or are you building an one pager why people should sponsor research that would be done by PCORnet?

DR. FLEURENCE: We had some very good conversations with industry. These are led right now out of our industry work group. We don't have hot promises yet because we also want to see what PCORnet is capable of doing. I think we still have a little bit of ground work to do with respect to getting all the nuts and bolts in place, including the data infrastructure piece, but also the IRB and

contracting processes, sort of being able to streamline these.

These conversations have started, and we think it is okay to start them early so by the time they come to fruition, we actually are able to support research studies.

I will say the individual networks themselves have already or are already supporting a fair amount of research studies, they are not the multi-site studies we talk about at the PCORnet wide level, but we have already made a large dent into sort of the capability of these networks.

Back to sort of Rick's comment, I think we do need a business development capability for PCORnet, but may not be sort of the bread and butter of academic centers, so I think we need to think really seriously about how we implement that piece, but it is built into the PWC recommendations. The one pager is critical, I agree with you, and we will need to get that done in short order.

CHAIRMAN NORQUIST: Sharon and then Gail.

DR. LEVINE: The contractual consortium, does that represent [inaudible]. Is that intended to be core funded?

DR. FLEURENCE: I need to be clear that the PWC recommendation right now is just a recommendation, so we have not had sort of a robust process yet for PCORI leadership to review it for the RTC and for the PCORnet stakeholders to review it.

The current recommendation is for the contractual consortium to be built off membership fees that would go from probably three to five years, and then actually would possibly go away with the increased volume of research that we would be able to support potential functions.

That is the proposal on the table.

CHAIRMAN NORQUIST: Gail and then Christine.

MS. HUNT: I'm following up on Bob and also Sharon's comments. I'm wondering what the business case will be and what is the tie of the business case of PCORnet to PCORI. Will there be

more than one PCORI representative as a voting member on the Council versus our having -- are we taking on some kind of additional fiduciary responsibility that would be a part of the consortium model, so that we would be perhaps liable if things didn't turn out the way there was contractually the expectation? That's one thing.

I guess I'm sort of -- I know a little bit about the for profit side. I'm not sure that I see in a relatively short period of time that PCORnet will be able to establish a robust enough backlog of research projects that it will be able to sort of exist on its own.

When will we have the opportunity to see exactly what PWC is proposing? I know that doesn't mean we have adopted it. I'm just saying. There are lots of business questions around this, leaving aside the research questions.

DR. FLEURENCE: Yes, there are a lot of points in your question. Thank you for making them. I should have said this to Sharon as well. I think a lot of the PWC work is around building a

value proposition for the participating networks within PCORnet. There has to be something in it for the CDPNs and the PPRNs to pay membership fees, so that is a lot of our work now and a lot of our work with PWC will be to make sure PCORnet is set up for these institutions to be willing and find something in it for themselves to continue participating.

In terms of the fiduciary requirements, PCORI's legal department is looking very closely at that, and is really ensuring there will not be liability for PCORI where there doesn't need to be liability for PCORI.

A lot of the consortium will be set up in a way and a structure that really ensures that PCORI has the right relationship with the future structure. I'm very confident our legal department and external counsel are looking at that closely and it will be set up under the appropriate process.

I think you asked about when we would see the PWC recommendations. We currently have a draft

version of that. It needs to be vetted by PCORI leadership and undergo some legal review for the reasons you just brought up, make sure the structure is appropriate in terms of what PCORI can and cannot do.

Joe and I will present it more fully to the RTC, which is the committee that oversees PCORnet, and I'm sure there will be some way to present it to the Board as a whole, what the recommendation is for PCORnet.

There is going to be quite a bit of work, I think, over the fall, familiarizing ourselves and then the PCORnet stakeholders with this report and recommendations. They also have to buy into whatever is being proposed. Otherwise, it won't work.

I hope I answered all your points.

CHAIRMAN NORQUIST: Christine?

MS. GOERTZ: Thank you, Rachael. I'm in awe of the huge amount of work that has gone into this over the last couple of years. It truly is extraordinary.

I'm wondering what the timing is with the NIH collaboratory fund, and the end of our commitment toward infrastructure building. It seems like they are not exactly happening at the same time, and if any thought has gone into how that might impact your business plan.

It seems not only our network but the collaboratory is going to be somewhat scrambling for sustainability in the same time period. I'm just wondering if you have thought about that.

DR. FLEURENCE: We have not thought about it specifically as to the NIH collaboratory fund. That might be something for us to consider as we look through the business plan recommendations.

I think essentially now our priorities are to think about what this structure might look like and then make sure we do have this business development function so that we can bring in research from a number of different parties to support PCORnet networks.

I think a little differently from the NIH collaboratory, which is really built upon sort of

the seven to ten pragmatic trials, that we are really funding networks who themselves are able to be able to bring in research themselves, so they are ready sort of individually being able to find ways to be sustainable and sustain themselves, and that was also part of their Phase II applications.

We always have to think about sort of the network level and then the PCORnet wide level. We are largely focused on the PCORnet wide level and how to launch the consortium, but each network itself is thinking about it, sustainability and how it may sustain research based on the infrastructure that we have helped build.

DR. SELBY: I think part of the challenge for us is to direct their thinking about sustainability toward a PCORnet wide sustainability rather than sustaining predominately their own network.

DR. FLEURENCE: Right.

DR. SELBY: It has to be both.

MS. GOERTZ: That's why I'm thinking about it in the sense that the timing is such and since

they're going to be a lot of the same people trying to figure out, they may even have competing demand, some competing priorities.

CHAIRMAN NORQUIST: Sharon?

DR. LEVINE: You said "leading with industry." I just wondered specifically which industry you were talking about.

DR. FLEURENCE: We met in March with the pharmaceutical, device, and diagnostic industries. We had a two day workshop. Out of that came a work group that has both stakeholders from these particular life science industries but also from the FDA and PCORI and probably a few others, just trying to figure out what the plan moving forward will look like, what the requirements are to support research within PCORnet, what the processes are, et cetera.

DR. LEVINE: The reason I asked is I suspect there might be equal interest on the part of the carriers as an industry group to get some of their questions answered.

DR. SELBY: We have an ongoing project

with payers. We have convened one face to face meeting and now we are planning a second one. Also, the funding announcement to attract two large payers is another part of that strategy. The reason it is two is we realize it has to be proved it can be done, and we think having two attempts at that is probably enough right off the bat. It may prove successful and advisable to link up with other plans, and then once the plans are involved, this notion of discussion between plans and delivery systems and even plans and delivery systems and industry sponsors of research, pharmaceutical industry sponsors of research, is a very interesting prospect.

UNIDENTIFIED: I think it is really fascinating and fabulous work. I am sure you all have thought about it a lot. This whole process is fraught with peril from a potential ethical point of view. I guess I'm wondering -- this question is not necessarily to you, Rachael, but I think you did start to address the process, but I'm really curious as to whether there will be an opportunity

for us to discuss this at more length, the issue of governance and the issue of safeguards.

I think it is really important to get this right and not to get it right from the beginning, I'm sure, I can see how hard and thoughtfully people are working on it, but I wonder for the Board when we will talk about this and when we will hear presentations.

CHAIRMAN NORQUIST: Yes, we will have an opportunity. The question I would pose to Rachael is when is the right time or when do you want to have that conversation.

DR. FLEURENCE: We have a large stakeholder meeting planned in January, around what we are calling public trust, public trust worthiness, around PCORnet, and then engaging a number of groups to work through some of the ethnical implications with PCORnet, so perhaps after the January meeting would be a good time.

CHAIRMAN NORQUIST: Let's just plan on that. That will be an action item, Joe? Come back after that with a formal presentation and

discussion. Is that good?

DR. SELBY: Very good. Briefly, it is certainly a discussion that needs to be had. I guess it was at the May meeting that we had a discussion about whether in principle we wanted to support the development of some non-PCORI thing. This isn't the first time we have been through this, although as we get closer, all the issues need to be dealt with.

UNIDENTIFIED: Absolutely, this is a friendly remark, which is it is all in the details. I think we are all very happy about PCORnet and see that as one of the great potential legacies of PCORI.

DR. SELBY: I think this whole discussion has helped to focus -- Rachael and I certainly were aware of this before, but helped to focus having made the decision that we did at the last Board meeting that Rick points out, how you actually do that.

One of the things we know is that we may not have any more funding to give out coming come

the end of 2018 to sustain PCORnet even if we wanted to. It has been our judgment at the Board that we need to stimulate this sort of gradual separation from PCORI into its own entity.

The fine points about when you relinquish "control" are delicate and nuanced. If you hold onto control too long, you both risk ruining something that otherwise might have taken off, and you also risk maybe delaying the point at which the network really does make its own efforts to stand on its own two feet. It's quite delicate.

We sure hear, I think, your concern that we don't want this investment going to something that we really wouldn't be happy with on day one.

CHAIRMAN NORQUIST: Bob Zwolak.

DR. ZWOLAK: Very quickly, PCORI has made just enormous contributions to starting this project and funding these two pilot projects. I think one thing maybe we should talk about some more is whether we should fund more PCORnet directed research. I think I've heard comments and opinions on both sides of that issue.

One group is saying oh, no, if we offer research money, it should be to whoever offers up the very best application, and others suggesting we may need to give it some more seed money just to make sure it gets out of the net.

I think that's an important question.

CHAIRMAN NORQUIST: That is something we can discuss. I think it's a very important question. One thing I need to say right now because it's 5:30, I do need to let everybody know that as no one is present or waiting on the line, we will not be initiating our public comment period. You are always welcome to give us feedback at info@PCORI.org or through our website at PCORI.org.

We will finish up on this. Rachael, since we are still in public session, we have gotten some questions -- I have and some others -- about these various registries. What is the interface with those, any discussion about how they might interface? It has come up and I was just curious.

DR. FLEURENCE: The future interface with

registries is really important and we have put a lot of work into standardizing our data using a common data model and through the work, outreach to registries to see how we might collaborate, I think, is going to be very important.

We do have a number of registries within PCORnet, some PPRNs that came in as registries, and then sort of launched into patient-powered registries, if you will, with patient governance. We both have kind of models within PCORnet for registries to work with us, and then I think for future collaboration with registries, I'd say you have seen the work streams, I think the registry work stream has sort of just been a little further down the road so we could stress kind of the burning work streams.

We definitely see the future with registries as bright and we would like to be able to implement that.

CHAIRMAN NORQUIST: I think the point of that is as we develop the one pager, what is unique about what PCORnet would be doing as opposed to all

these other kinds of data infrastructure things, and then where are the collaborative efforts, so that people who are not as into this will understand what the differences are and the similarities and where the opportunities are.

Let me offer -- Freda, since you are the RTC chair, if you wanted to say anything at this point. Are you rock and rolling? I guess not.

[No response.]

CHAIRMAN NORQUIST: Anyone else on the phone?

[No response.]

CHAIRMAN NORQUIST: Thank you very much, Rachael, for that.

[Applause.]

DR. KRUMHOLZ: Gray, I just want to say one thing. Sorry if you hear this background noise. I do want to say it's an extraordinary job that Rachael has done. The point Alicia made I think is so important. It is all on us, not on anyone who put together PCORnet because when we developed it, we put them in the position where

this was going to be an issue. We don't want to have put in all this money just to start a CRO.

It's going to be something we need to struggle with them because they now have an active group that has been investing a lot, and I think it is a high priority for us to spend a lot of time talking about how we can best interface with them. We want them to be independent, but we also want them to adhere to our principles, and I think that is a very tough line to walk. We want them to be able to get their own sources of revenue but we want them to act in certain ways. I think it is one we are going to have to work together to try to solve.

CHAIRMAN NORQUIST: I agree, like having a child, you want them to be independent but at the same time you want to direct it.

CHAIRMAN NORQUST: Thank you, Rachael, very much. One of the things we have been trying to do, and starting with this meeting, was to be clear as we had action items or things to follow up on, because I've asked Joe and them that as things

came up, we wanted to make sure we had follow up, and then at the next Board meeting, we had a report on how we followed up on that.

I would hope people would help us with ones we missed, but we have a list of them that we kind of pulled as we went through today. Joe?

MR. SELBY: I'm so glad you asked. Listen carefully and let us know if we missed any. Back to the earliest discussions this morning, there is a strong call for more evidence about the milestones and active portfolio management, what do we do when projects approach and enter the red zone, how long, for example, do we go before termination.

We have had some e-mail exchange during the day with people from staff who were listening in, confirming what we said this morning, we have excellent SOPs in this area and good practice on this, but we will report back to you in detail at the December Board meeting. That is part of the December Dashboard report.

A good point was made, somehow you can't

just change/modify contracts, delay milestones, and then report that everything is okay, or else you could manage to have 100 percent excellent performance even though nothing ever got done.

We will work toward and get back to you on that, too. We have a little bit there, but we need to get it more linked to the performance reports, we are this good, but that links to X number of contract modifications and delays. We think that through a little bit more carefully.

We will provide more information about application success rates, particularly more information on resubmissions, how they fare, and how our success rates for resubmissions may compare with those at AHRQ and NIH.

Also, the question about how likely are unfunded applicants to reapply. We will take that under advisement. Remember we report back to you in two weeks on what we are doing. We will try to have a report back to you by then on who is going to handle that and when we can get back to you.

We are going to modify the presentation of

studies proposed for funding at least to the extent that we give you clear information on the intervention arms that are being compared. That was missing from two of the big studies today.

In general, I think I heard the Selection Committee vowing to work a little more detailed into the slate presentation and the rationale. I think this has more to do with the pragmatic trials, the bigger studies than the smaller ones. We had some good discussion today even about the broad slate.

Next was we commit to working on pursuing the idea of a question around opioid therapy, which has to do with primary prevention of chronic opioid therapy use. We will explore this with advisory panels, with the SOC, and with NIDA, and keep you apprised of that. Again, we will have a plan in a couple of weeks.

Gail's call to really gear up dissemination now that the results are starting to pour in was heard, and I think the next meeting would be a good time to update you on hiring and

other activities around dissemination that are picking up, so we will be glad to report back to you on that in December.

An interesting question was whether the Methodology -- this was Harlan Kromholz -- the Methodology Committee actually needs its own website or a more obvious expanded spot on PCORI's website. Also, are there additional ways that we can work on developing handy tools for people to use, both in doing research and in training and education.

The next one was about PCORnet and the questions were raised about the extent, nature and quality of patient and stakeholder engagement in PCORnet. You asked about an opportunity to speak with or to hear more about this, and I think what we should commit to is getting the Executive Committee of PCORnet, which brings the coordinating center along, to talk to you about our engagement plans in Phase II, as the best way to do that.

I agree with whomever said we simply need to look for more opportunities to interface, we

realize, just like Gray said, you need to look for opportunities to interface with your teenaged children, and this is very similar here.

The idea of one pagers that was actually raised first by Lew Sandy but then Harlan rephrased it with respect to PCORnet. In fact, we have one pagers and we use them, particularly on the Hill, we use them. When we have guest stakeholders coming, we have an one pager on PCORnet, an one pager on pragmatic studies, an one pager on the broad and overall PCORI portfolio. I think they are actually quite wonderful.

What I did hear is we should probably build into these a little bit more about what the future holds, where these are leading to, what they can actually do. Right now, they are a little more matter of fact, a little bit more objective. They are not maybe as forward looking or as conveying of the promise of this effort as they could be.

Those are the ones I captured. Does anybody have another one that they suggested? You usually remember the ones you suggested best.

DR. LEVINE: I have one I didn't suggest. It was a thought that came to me as we were talking pretty much through the day, it is the issue of looking at the opportunity we have in systematic reviews, landscape reviews, systematic reviews, and whether we might do some anticipatory work.

DR. SELBY: Did Evelyn plant that question with you?

DR. LEVINE No, I didn't even talk to her about it.

DR. SELBY: You know she is a national leader in that work. We definitely anticipate more in evidence synthesis in general and also synthesis of our own research, and also the topic brief.

DR. LEVINE: My point is we are at a point now where I suspect we can anticipate some of the research questions that we will want to pursue over the next three years. Doing some systematic reviews as a basis of jump starting some of that work as the development of PSAs happen. It might be useful.

DR. SELBY: Excellent. It is actually

something we are thinking about a lot. We talked a lot with AHRQ about it, too, because they do a lot of evidence synthesis. We have already begun talking about it with Evelyn. I think she will really energize that work here at PCORI, thinking about it. We may postpone the report back a little bit beyond the December meeting because she won't be with us yet in December.

DR. LEVINE: A related topic, and we discussed it at the Governance Committee, the issue of looking at as part of a Board development activity -- I hope this is all right to raise this before your report.

Looking at the state-of-the-art of health services research into health systems improvement, doing some work on that and using that as a Board development. I think there have been questions about whether we should continue that stream of research, whether we ought to enhance it, are we picking the right topics around improving health systems. I think as part of Board development work with a systematic review on the topic of what the

state of the research is into that internet arena might be helpful for the Board and helpful for us to evaluate our portfolio.

CHAIRMAN NORQUIST: Bob?

DR. ZWOLAK: Joe, just as a reminder, I would like to hear more discussion about this topic related to PCORnet, specifically fund additional PCORnet research projects or prioritize, give a weighted score to PCORnet involvement or just let them fight among all other competitive bidders.

DR. SELBY: One argument is with all the resources and infrastructure we have funded, they ought to be competitive. One thing that occurred to me when Gray asked, there might be some kind of role for supporting particularly projects where other registries link with PCORnet. That might be an area.

CHAIRMAN NORQUIST: Others on the phone?

[No response.]

MS. GOERTZ: I would just say to follow up on Alicia's idea about the toe in the water concept of trying to provide opportunities for

investigators to potentially be engaged in pilot projects or some small comparative effectiveness research to get their interest.

CHAIRMAN NORQUIST: Okay. Thanks. Let me close by thanking those who joined us today both in person as well as via webcast, teleconference. A reminder, our materials will be soon available on the website at PCORI.org. We always welcome your feedback at info@PCORI.org or through our website.

Thanks for joining us, and good evening to everyone. Thanks.

[Whereupon, at 5:45 p.m., the meeting was adjourned.