

Board of Governors Meeting via Teleconference/Webinar

April 30, 2018

10:15 am - 5:45 pm ET



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Welcome and Introductions

Grayson Norquist, MD, MSPH

Chairperson, Board of Governors

Joe Selby, MD, MPH

Executive Director



Time	Agenda Item
10:15-10:20	Welcome and Call to Order Consider for Approval: Minutes of March 20, 2018 Board Meeting
10:20-11:00	Executive Director’s Report
11:00-11:30	Consider for Approval: Dissemination and Implementation PFA Development
11:30-12:00	Methodology Committee Update - Consider Adoption of New Methodology Standards
12:00 – 1:00	Lunch
1:00-2:00	Stakeholder Panel: National Multiple Sclerosis Society and The Michael J. Fox Foundation for Parkinson’s Research
2:00-3:00	Consider for Approval: Pragmatic Clinical Studies and Targeted Awards Cycle 2 2017 and Cycle 1 2017
3:00-3:15	Break
3:15-3:45	Consider for Approval: Targeted PFA Development Psychosocial Interventions with Office-Based Opioid Treatment
3:45-4:45	PCORnet Update: ADAPTABLE, Searchable Tool, Dashboard Metrics
4:45-5:15	Consider for Approval: Partnerships to Conduct Research within PCORnet (PaCR) Awards Cycle 2 2017
5:15-5:45	Public Comment
5:45	Wrap-up and Adjournment

Board Vote

Call for a Motion to:

- **Approve** the Minutes of the March 20, 2018 Board Meeting

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Voice Vote:

- Vote to **Approve** the **Final** Motion
- Ask for votes in favor, opposed, and abstentions



Executive Director's Report

Joe Selby, MD, MPH

Executive Director



GAO Highlights

Highlights of GAO-18-311, a report to congressional committees

Why GAO Did This Study

In 2010, the Patient Protection and Affordable Care Act (PPACA) authorized the establishment of PCORI to carry out CER and improve its quality and relevance. PPACA also established new requirements for HHS to, among other things, disseminate findings from federally funded CER, including findings published by PCORI; and coordinate with relevant federal health programs to build data capacity for this research. To fund CER activities, PPACA established the Trust Fund from which PCORI and HHS are expected to receive an estimated \$4.0 billion from fiscal years 2010 through 2019.

PPACA included a provision for GAO to review PCORI's and HHS's use of the Trust Fund. This report examines (1) PCORI's use of the Trust Fund for CER activities, including the dissemination and use of research findings; and (2) HHS's use of the Trust Fund for these activities.

GAO examined PCORI and HHS documents and data related to use of the Trust Fund, such as commitment, obligation, and expenditure data; PCORI's audited financial statements; and descriptions of CER activities. GAO also interviewed PCORI and HHS officials responsible for planning and carrying out CER activities and interviewed officials from stakeholder organizations representing potential users of CER, including public and private payer organizations, provider organizations, and patient organizations. PCORI and HHS provided technical comments, which GAO incorporated as appropriate.

View GAO-18-311. For more information, contact John E. Dicken at (202) 512-7114 or dickenj@gao.gov.

March 2018

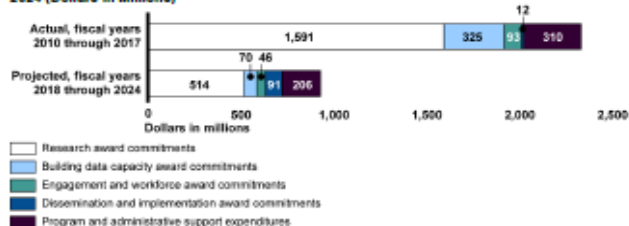
COMPARATIVE EFFECTIVENESS RESEARCH

Activities Funded by the Patient-Centered Outcomes Research Trust Fund

What GAO Found

The Patient-Centered Outcomes Research Institute (PCORI) made about \$2 billion in commitments for awards in fiscal years 2010 through 2017. PCORI is a federally funded, nonprofit corporation established to carry out and improve comparative clinical effectiveness research (CER), which evaluates and compares the health outcomes and the clinical effectiveness, risks, and benefits of two or more medical treatments, services, or items. PCORI provides funding through award commitments from the Patient Centered Outcomes Research Trust Fund (Trust Fund) and may pay these awards over multiple years. Of the \$2 billion PCORI committed as of the end of fiscal year 2017, about \$1.6 billion (or 79 percent of its commitments) is for research awards, and \$325 million (or 18 percent) is for building the capacity to use existing health data for research. Through fiscal year 2017, commitments for dissemination and implementation awards—intended to share CER findings with potential users of this research—were limited because most PCORI-funded research was still underway. PCORI projects to commit an additional \$721 million for awards in fiscal years 2018 through 2021. In addition to awards, PCORI spent \$310 million on program and administrative support services in fiscal years 2010 through 2017 and projects to spend an additional \$206 million for these services through fiscal year 2024.

PCORI's Actual and Projected Commitments and Expenditures, Fiscal Years 2010 through 2024 (Dollars in Millions)



Source: GAO analysis of Patient-Centered Outcomes Research Institute (PCORI) information. | GAO-18-311

Note: Amounts listed are current as of Jan. 5, 2018.

From fiscal years 2011 through 2017, the Department of Health and Human Services (HHS) obligated about \$448 million from the Trust Fund. Of this amount, HHS obligated about \$260 million (or 58 percent of all obligations) to the dissemination and implementation of CER findings. As most PCORI-funded CER had not yet been completed due to the time needed to conduct this research, HHS efforts focused instead on the dissemination and implementation of CER funded by other federal entities. Additionally, HHS obligated funds for efforts to train researchers on conducting CER, build data capacity, and on administrative activities. HHS projects to obligate an additional \$120 million for these activities in fiscal years 2018 through 2020.

United States Government Accountability Office

PCORI's 8-Year GAO Report has been published!

“

PCORI Committed Funds Primarily to Research and Data Capacity Efforts; Awards for Dissemination and Implementation of Findings Were Limited as Most Research Was Still Underway

“

Officials from most stakeholder organizations we interviewed generally agreed that PCORnet offers value by improving the data available to conduct CER

“

PCORI research awards have increasingly focused on conditions that impose a substantial health or financial burden on patients and the healthcare system



PCORI-Funded Research Results Highlights



PATIENT-CENTERED OUTCOMES
RESEARCH INSTITUTE

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Highlights of PCORI-Funded Research Results

Since PCORI began funding research in 2012, a growing number of our funded studies have produced important results that are being reported in leading medical journals. Here are examples:

For Many with Type 2 Diabetes, Daily Finger Sticks Offer Little Health Benefit

People with type 2 diabetes who are not using insulin are often advised to check their blood sugar levels using daily finger sticks, which can be painful, inconvenient, and run up out-of-pocket costs for test strips. This study suggests that for these patients, daily self-monitoring does not help control diabetes or delay the need to start insulin compared with not doing so.

Young L et al. *JAMA Intern Med*. 2017 Jul 1; 177(7)

Over five years,
10 BILLION
finger sticks could
be avoided

with usual care. These nondrug approaches can help manage chronic pain and reduce the need for opioids, and these findings show they can be effective even in patients with low incomes and limited reading skills.

Thorn B et al. *Ann Intern Med*. 2018 Apr 3;168(7)

Oral Antibiotics Work as Well as IV with Fewer Costly Complications

In preventing a recurrence of infection, children discharged from the hospital after a serious bacterial infection did just as well on oral antibiotics as those sent home with an IV line to deliver antibiotics intravenously. They also had none of the frequent complications IV lines can cause after being in place for weeks.

Keren R et al. *JAMA Pediatr*. 2015 Feb; 169(2)

Shah S et al. *Pediatrics*. 2016 Dec; 138(6)

Rangel S et al. *Ann Surg*. 2017 Aug; 264(2)

Initiative to Reduce Risky Opioid Prescribing Works

This study compared rates of opioid use in clinics in Washington state that implemented an initiative focused on more cautious prescribing of opioid drugs with clinics that did not use such strategies. This health system-based initiative led to reductions in high-dose opioid prescribing, and patients did not report worse pain control.

Von Korff M et al. *J Pain*. 2016 Jan; 17(1)

Disadvantaged Patients with Chronic Pain Benefit from Simplified Nondrug Therapies

Chronic pain occurs more frequently in people with lower education and income levels. In this study, both cognitive behavioral therapy (CBT) and pain education material, each tailored to match patients' education levels, significantly lessened pain and improved physical function compared

Simple Questionnaire Enhances Shared Decision Making about Chest Pain

A questionnaire called Chest Pain Choice can help people who go to the emergency department with chest pain, but who are found to not be having a heart attack, decide whether to be admitted to the hospital for follow-up tests or go home and have the tests later. People who used the aid were much more likely to go home from the emergency department, with no greater rate of later heart-related problems.

Hess E et al. *BMJ*. 2016 Dec 5; 355

Over five years,
9.4 MILLION
Americans could
benefit from using
the decision aid



For Many with Type 2 Diabetes, Daily Finger Sticks Offer Little Health Benefit



Oral Antibiotics Work as Well as IV with Fewer Costly Complications



Simple Questionnaire Enhances Shared Decision Making about Chest Pain

Strategic Plan Update: Address stakeholder needs in relation to new therapeutics and new technologies

- PCORI will establish a Horizon Scanning Program by 12/31/18
 - Horizon scanning identifies and monitors target technologies and therapeutics in healthcare
 - A robust Horizon Scanning process helps payers, patients, clinicians, researchers, and PCORI identify and monitor important new therapeutics and technologies before they enter the market
 - A framework is developed for forecasting which target technologies have the highest potential for impact on clinical care, healthcare delivery, patient outcomes and cost
 - Horizon Scanning also serves to identify key research questions that PCORI can address as the technologies enter the market



Link Horizon Scanning with other Information on Emerging and New Technologies and Interventions

- PCORI is beginning to generate new products to provide useful, timely information for patients, clinicians, and payers on new drugs /devices (e.g., from horizon scan reports to brief topic brief summaries, evidence mapping, and more in-depth evidence syntheses, as appropriate)
- These “pre-PCORI research” topic brief summaries are intended both to meet information needs and to inform more definitive research
 - The content is being developed with stakeholder input, but clearly will include:
 - “Patient-centered outcomes,” disruptions, and comparisons that need to be addressed in order to measure value
 - Any on-going studies, including patient populations, settings, etc.
 - Regulatory and policy environment
 - Tying these products to further research priorities and development would enhance their value for decision makers, as the clear lack of evidence for many new technologies is the problem



Next Steps

- PCORI already produces Evidence Updates for patients, clinicians, and policy makers based on systematic reviews – **ongoing**, next Evidence Update on Treatments for PTSD
- PCORI is currently developing its first Briefs on new and emerging technologies and interventions – **started April 2018**, first brief on CRISPR and CAR-T expected in six months
- Award Horizon Scanning Program contract and begin implementation **before the end of 2018**
- Revitalize topic and research question priority setting and refinement using tools from Horizon Scanning, emerging topic briefs, evidence mapping, and consultation with stakeholders – **ongoing**
- Systematic consultation forums with patients, clinicians, and payers – **January/February 2018** and **June/July 2018**



Evaluation: Comparisons of PCORI and National Institutes of Health (NIH) CER Portfolios

Author(s):



*Heather Edwards,
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Program Officer,
Strategic Portfolio
Analysis
Evaluation and Analysis



*Laura Forsythe,
PhD, MPH*
Director, Evaluation
and Analysis
Evaluation and Analysis

Topics

[Research](#)

[Evaluating Our Work](#)



Uncovering How PCORI's Funded Research Is Different

Date: April 27, 2018

Blog Topics: [Research](#),
[Evaluating Our Work](#)

PCORI was created for one distinct purpose: to fund and support comparative clinical effectiveness research (CER) to better inform health decisions faced by patients, their caregivers, and their healthcare providers. And today, we are the only research funder solely focused on addressing the questions of these stakeholders using patient-centered CER.

One key way we have sought to achieve our mission is by engaging patients and other stakeholders at every stage of the research process, from generating the research questions to developing research proposals, serving on the panels that evaluate the research proposals we receive to be sure they're truly patient-centered, and participating on research teams as studies are conducted. Compared with other health research, our approach should enhance the relevance of the research questions and the findings, improve participant recruitment and retention during the study, and speed up translation of results into practice.



From our early days, [we've worked](#) to evaluate whether our efforts are making a difference. A direct comparison of PCORI-funded research to similar studies funded by others would be the most straightforward way to know whether our approach not only is different, but in fact leads to different results. Now that we have funded more than 400 CER studies, a substantial number of which are completed or nearly so, we can take a clear look at how our research portfolio is unique and complements that of other funders.



We will conduct a series of analyses that compare PCORI and NIH CER portfolios



Comparisons	Examples
Portfolio characteristics (Expected completion in fall 2018)	types of interventions, conditions studied, outcomes measured
PI and institution characteristics	discipline, specialty, years experience
Study efficiency	recruitment, retention, changes to primary completion date
Study dissemination and impact	altmetrics, bibliometrics



Inclusion Criteria for Studies

	PCORI CER Studies	NIH CER Studies
Project type: CER study	- Research awards made under Assessment of Prevention, Diagnosis, and Treatment Options, Addressing Disparities, Improving Healthcare Systems, and Communication and Dissemination Research	- Grants with CER Research, Condition, and Disease Categorization tag - Research projects (e.g., not infrastructure, training, or other capacity building)
Funding activity	- Broad, Pragmatic Clinical Studies, and Targeted studies	- R01, U01, U10, P30, P50, P01 activity types* - NIH defined announcements and parent announcements
Time period	- New studies funded between FY-2013 and FY-2016	- New studies funded between FY-2013 and FY-2016
Study design	- All study designs (trials, observational studies)	- All study designs (trials, observational studies)

*All R01 studies with the CER tag will be included in the analysis. Studies associated with the other activity types will be reviewed to determine if they align with PCORI's definition of CER.

Note: Some data elements can only be analyzed for the subset of projects that are registered in ClinicalTrials.gov. An exploratory review found that approximately 90% of studies are registered.



First Analysis: Portfolio characteristics

Use publicly available data (PCORI study pages, NIH RePORTER, clinicaltrials.gov) to describe CER studies funded by each organization

- Type of funding opportunity
- Institute or Center (NIH only)
- Study duration
- Study cost
- Study design
- Estimated enrollment
- Conditions
- Primary purpose (e.g., care continuum)
- Intervention type (e.g., drug, device)
- Type of CER question (e.g., comparison of treatment strategies, practical questions)
- Outcomes
 - Number to be studied
 - Domains (e.g., clinical, health status and well-being)
 - Specific outcomes



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Farewell and Best Wishes

Thank you, Dr. Evelyn Whitlock,
for your leadership and scientific
contributions towards advancing
PCORI's mission.



Implementation of Evidence from Major PCORI Research Investments

Request for PFA Development Approval

Larry Becker

Engagement, Dissemination, and Implementation Committee

Jean Slutsky, PA, MSPH

Chief Engagement and Dissemination Officer



Consistent with PCORI Authorizing Law

*“The purpose of the Institute is to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed through research, and evidence synthesis that considers variations in patient subpopulations, **and the dissemination of research findings.....**”*



The Proposed PFA within PCORI's Dissemination & Implementation Program

- The Dissemination and Implementation Program is charged with heightening awareness of the results of PCORI-funded research, and **with advancing efforts to put these findings into practice** to improve healthcare delivery and health outcomes



Other PFAs supporting Dissemination and Implementation of Evidence from PCORI-funded Research

Limited Competition: Implementation of PCORI-Funded PCOR Results

- Provides PCORI investigator teams the opportunity to **propose the next steps** to put their findings into real world practice. (\$9M total funding available per year)

Implementation of Effective Shared Decision Making (SDM) Approaches

- Promotes the implementation and systematic uptake of shared decision making in practice settings. SDM approaches can be those previously studied in PCORI CER, or existing, effective SDM strategies (not PCORI-funded) that incorporate findings from PCORI research. (\$6.5-\$8M total funding available per year)

Eugene Washington Engagement Awards

- Organizations and communities can propose meaningful dissemination projects to spread awareness and increase knowledge of new evidence from PCORI-funded research, targeted directly to patients, clinicians, and others to inform healthcare decisions. (Within Engagement Award budget of \$20.5M per year)



PCORI Dissemination & Implementation Activities

PCORI Evidence Updates

CME/CE

Engagement Awards:

- Dissemination Initiatives
- Building Capacity for Dissemination
- Conference Support



Dissemination activities to bring results to audiences that will have a strong interest in using them



Implementation activities to change practice

Convening and Input from PCORI Stakeholders & Building Capacity of Communities and Others

NEW: Implementation of Evidence from Major PCORI Research Investments (Open)

Implementation Awards for PCORI Findings (PCORI Awardees)

Implementation of Shared Decision Making (Open)

AHRQ/PCORI Collaborative Projects



Background

- PCORI has made major research investments in a number of specific, high-impact research topics through Targeted PFAs, Pragmatic Clinical Studies, and PCORnet Demonstration Studies
- These research investments reflect priorities developed through a systematic topic generation and research prioritization process involving close collaboration with stakeholders
- Between 2018 and 2022, approximately 90 studies funded under these mechanisms will produce findings
 - These studies represent approximately \$800M in total PCORI investment

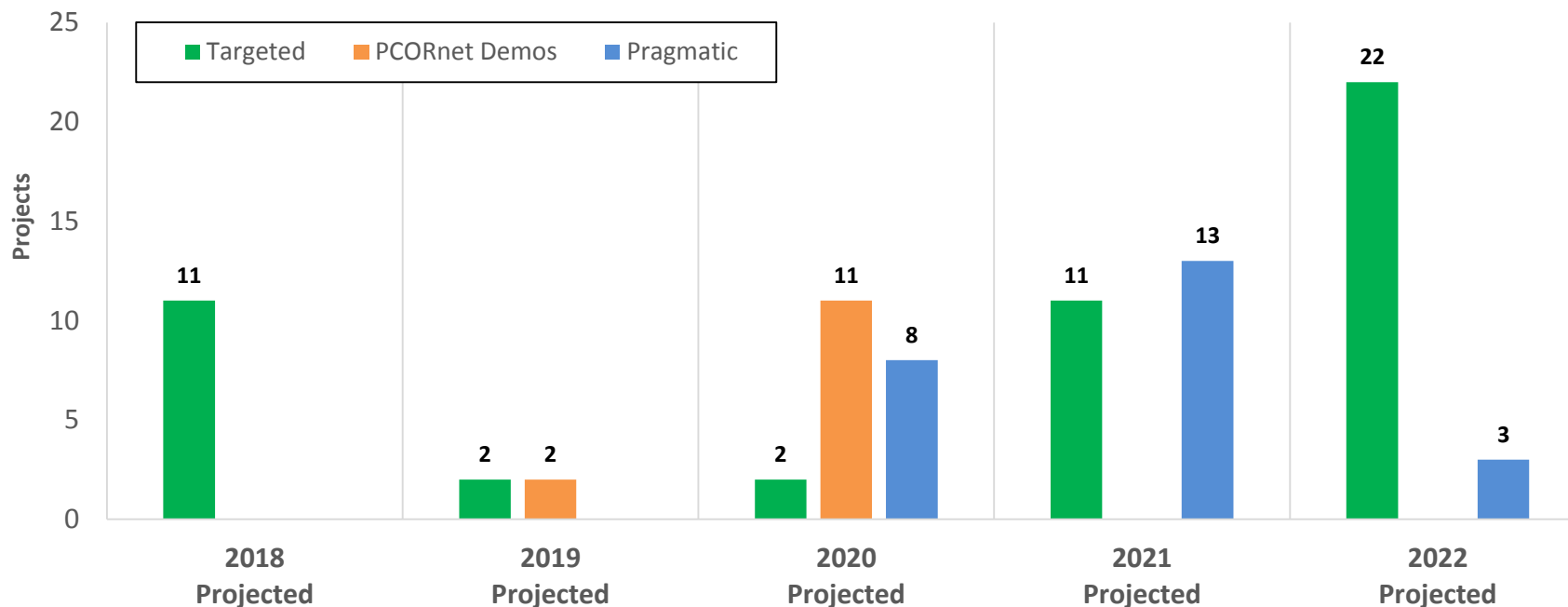


Purpose of Proposed Implementation PFA

- To support projects that facilitate the uptake of peer-reviewed clinical comparative effectiveness research **evidence from PCORI's major research investments**
 - *PCORI's "major investments" include Targeted PFAs, PCS, PCORnet Demonstration Studies*
 - *Findings from Broad Studies with **strong potential** for impact may also be the focus for implementation under this PFA*
- Through a **broad call for proposals**, to engage and draw on the expertise, creativity, and capacity of a large and highly diverse pool of applicants and implementers, in service of implementing these important findings
- With the end goal of promoting the uptake of peer-reviewed findings from high impact PCORI-funded studies at the point of care or in other decision settings



Estimated Timeline for Results from Major Research Investments



- Asthma
- Care Transitions

- Uterine Fibroids
- Fall Prevention
- Obesity Demos

- Obesity Treatment
- Opioid Prescribing
- MS
- Aspirin
- PPRN Demos
- Natural Experiments Network

- Hypertension
- Hepatitis C
- Palliative Care
- Opioid Use
- NOACs
- MS

- Sickle Cell
- Opioid Use
- Depression
- NOACs
- Palliative Care
- Atrial Fibrillation



Eligible Evidence for Implementation in this PFA

- Published, peer-reviewed evidence emerging from areas of major PCORI investment
 - Studies under PCORI **Targeted PFAs**
 - **Pragmatic Clinical Studies**
 - **PCORnet Demonstration Studies**
 - **Broad studies** with very strong potential for impact
- Each release of this PFA will identify selected areas, from among the eligible research, that PCORI will prioritize for implementation activities
 - This flexibility will enable us to promote collaboration and avoid duplication with AHRQ, when AHRQ selects PCORI CER findings as the focus of its own implementation activities



The proposed PFA will extend and complement existing Dissemination and Implementation Funding initiatives by:

- Providing a mechanism for PCORI to focus on findings from specific, high-priority initiatives
- Attracting a larger and broader pool of applicants, including implementation experts and diverse stakeholder partners, through an open competition
- Providing the opportunity to propose larger implementation projects to promote the uptake and integration of these findings



Funding Announcement Overview

PFA Release	Cycle 3 2018 (October, 2018)
First Awards Funded	Summer 2019
Max Project Budget	\$2.5M total costs
Max Project Period	Three years
Funds Available	Up to \$10M per cycle; 2 cycles per year. Note: Funds available will be adjusted in line with increasing availability of evidence from major PCORI research investments.
Applicant eligibility	This is an OPEN competition. Applicants may or may not have been previous recipients of PCORI awards. Standard organization eligibility criteria for PCORI awards apply.



Funding Announcement Requirements

All proposed implementation projects are expected to:

- Incorporate **active strategies** that will lead to uptake and integration of PCORI evidence into **real world practice** settings
- Target **specific end-users** who are committed and motivated to use the evidence
- Demonstrate **commitment and buy-in** from proposed implementation sites to improve healthcare quality and a willingness to invest in the evidence being implemented, such that they provide a supportive context and culture for undertaking the proposed project
- Work with **regional and national stakeholder organizations** who are positioned to extend the impact of PCORI evidence to broader venues



Funding Announcement Requirements (continued)

- Be **guided by an established conceptual model or framework** and, where possible, by evidence regarding effective strategies for implementing evidence-based practices and interventions
- Address **adaptation of findings** (to facilitate uptake in the proposed settings), **scale-up** (to reach larger numbers), and **scale-out** (to reach broader audiences), as applicable
- Include rigorous evaluation plans that document:
 - successful **execution of the implementation strategy**, and
 - **impact of the implementation project** on outcomes of interest, including measures of behavior change, healthcare utilization impacts, and impacts on health outcomes as feasible and appropriate within the project scope



Timeline

EDIC Endorsement of PFA Concept	March 13, 2018
Board of Governors Vote	April 30, 2018
Initiate formal PFA Development	May 1, 2018
Release PFA; Applicant Townhall	September/October 2018
Letters of Intent Due (Cycle 3 2018)	November 2018
Applications Deadline	February 2019
EDIC Review per Board-Approved Process	Summer 2019
Board of Governors Vote	Summer 2019



Board Vote

Call for a Motion to:

- **Approve** the development of a PFA for Implementation of Evidence from Major PCORI Research Investments, with funding up to \$10M in total costs per cycle and additional cycles not to exceed the Board-approved budget amounts for the D&I program.

Call for the Motion to Be Seconded:

- **Second** if further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Methodology Committee Update: Consider Adoption of New Methodology Standards

Robin Newhouse, PhD, RN

Chair, PCORI Methodology Committee

Steven Goodman, MD, MHS, PhD

Vice Chair, PCORI Methodology Committee



PCORI Methodology Committee

Consistent with PCORI's authorizing law, the Methodology Committee works to develop and improve the science and methods of comparative clinical effectiveness research

Methodology Committee Members:

- Robin Newhouse, Chair
- Steven Goodman, Vice Chair
- Naomi Aronson
- Ethan Basch
- Stephanie Chang
- David Flum
- Cindy Girman
- Mark Helfand
- Michael Lauer
- David Meltzer
- Brian Mittman
- Sally Morton
- Neil Powe
- Adam Wilcox



PCORI's Methodology Standards

- Required by PCORI's authorizing law
- Developed by the Methodology Committee and proposed to the Board for adoption after opportunity for public comment
- Represent minimal standards for design, conduct, and reporting of comparative effectiveness research (CER) and patient-centered outcomes research (PCOR)
- Provide guidance to researchers and those who use research results
- Reflect generally accepted best practices
- Used to assess the scientific rigor of funding applications and monitor conduct of research awards



Development & Adoption of New Methodology Standards

- Methodology Committee undertook a systematic process to draft, revise, and finalize six new Methodology Standards
- Board approved these standards for public comment (October – December 2017)
- Methodology Committee reviewed the public comments and revised the standards, as appropriate
- Methodology Committee approved the new standards to be brought to the Board for adoption
 - Standards for Studies of Complex Interventions (new category, 5 standards)
 - Data Management Plans (DMPs) (existing category, 1 new standard)



Proposed New Standards: Studies of Complex Interventions

Rationale:

- Additional guidance is needed to ensure the appropriate design, conduct, analysis, and reporting of studies of complex interventions, which are being studied with increased frequency in health services research

Titles of proposed new standards:

- **SCI-1:** Fully describe the intervention and comparator and define their core functions
- **SCI-2:** Specify the hypothesized causal pathways and their theoretical basis
- **SCI-3:** Specify how adaptations to the form of the intervention and comparator will be allowed and recorded
- **SCI-4:** Plan and describe a process evaluation
- **SCI-5:** Select patient outcomes informed by the causal pathway



Proposed New Standard: Data Integrity & Rigorous Analyses

Rationale:

- Data management plans (DMPs) are critical to ensuring the scientific integrity of clinical research and facilitating data-sharing efforts

Titles of new standard:

- **IR-7:** In the study protocol, specify a data management plan that addresses, at a minimum, the following elements: collecting data, organizing data, handling data, describing data, preserving data, and sharing data



Next Steps

- Methodology Committee is recommending that the Board adopt six new Methodology Standards today
 - Updated Methodology Standards will include a total of 54 standards in 13 categories
- Upon adoption, the new Methodology Standards will be implemented for the Cycle 2 2018 funding cycle
 - PCORI will update the Methodology Report (expected June-July 2018)
- Methodology Committee is continuing work on other Methodology Standards
 - Data quality
 - Individual participant data meta-analysis (IPD-MA)
 - Qualitative and mixed methods



Board Vote

Call for a Motion to:

- **Adopt** six new PCORI Methodology Standards:

Standards for Data Integrity & Rigorous Analyses

- **IR-7:** In the study protocol, specify a data management plan that addresses, at a minimum, the following elements: collecting data, organizing data, handling data, describing data, preserving data, and sharing data.

Standards for Studies of Complex Interventions

- **SCI-1:** Fully describe the intervention and comparator and define their core functions.
- **SCI-2:** Specify the hypothesized causal pathways and their theoretical basis.
- **SCI-3:** Specify how adaptations to the form of the intervention and comparator will be allowed and recorded.
- **SCI-4:** Plan and describe a process evaluation.
- **SCI-5:** Select patient outcomes informed by the causal pathway.



Board Vote

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Break

We will return at 1:00 pm ET



**Join the conversation on Twitter via
@PCORI**



Stakeholder Panel: National Multiple Sclerosis Society and The Michael J. Fox Foundation for Parkinson's Research



Panel



Gail Hunt

Moderator

PCORI Board Member



Bari Talente, JD

Panelist

Executive Vice President, Advocacy

National Multiple Sclerosis Society



Sohini Chowdhury, MA

Panelist

Deputy Chief Executive Officer

The Michael J. Fox Foundation for Parkinson's Research



Pragmatic Clinical Studies

Cycle 2 2017 Award Slate

Christine Goertz, DC, PhD

Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH

Chief Science Officer



Cycle 2 2017 – Pragmatic Clinical Studies

Merit Review Criteria

1. Potential for the study to fill critical gaps in evidence
2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
3. Scientific merit (research design, analysis, and outcomes)
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder engagement



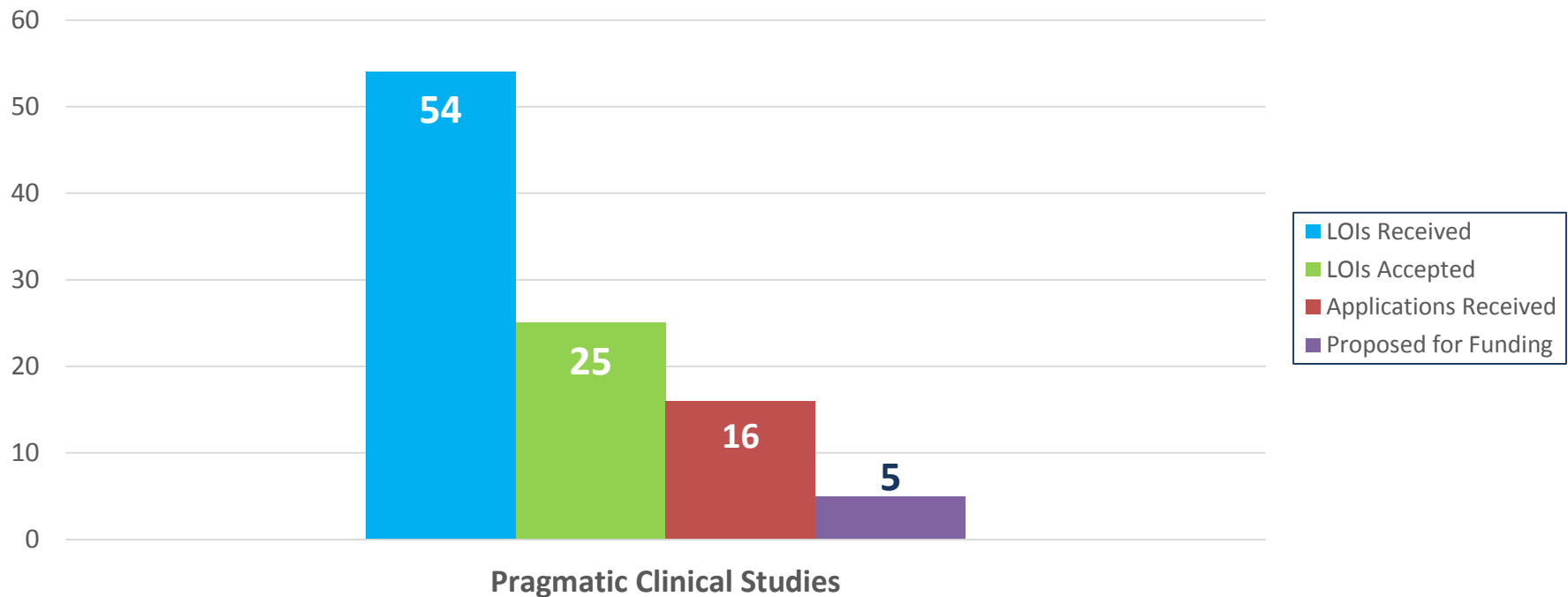
Cycle 2 2017 – Pragmatic Clinical Studies

Process Overview

- 54 Letters of Intent (LOIs) submitted
- 25 LOIs invited to submit a full application (**46%**)
- 16 applications were received (**64% of invited LOIs**)

Funding rate is 31 percent

- We are proposing to fund 5 applications* out of 16 received applications



Cycle 2 2017 – Pragmatic Clinical Studies

*5 Recommended Projects**

Project
A Pragmatic Family Centered Approach to Childhood Obesity Treatment (\$13.9M)
Comparison of Two- versus Three-Antibiotic Therapy for Pulmonary Mycobacterium Avium Complex Disease (\$6.2M)
Integrated Physical and Mental Health Self-Management Compared to Chronic Disease Self-Management (\$7.5M)
Multi-Level Interventions for Increasing Tobacco Cessation at FQHCs (\$9.8M)
KIDS FACE FEARS: Face-to-Face versus Computer-Enhanced Formats Pragmatic Study of Anxiety (\$13.6M)

Resubmissions in Bold

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Project 1: A Pragmatic Family Centered Approach to Childhood Obesity Treatment

- **Research Question:** What is the comparative effectiveness of two clinical treatment options—the staged approach versus the more initially intensive family-centered approach, at reducing weight among underserved children and their parents, within the primary care setting?
- **Population:** Children (ages 6-15) and their parents; low income
- **Intervention:** Staged treatment plus Family-Based Treatment
- **Comparator(s):** Enhanced usual care
- **Outcomes of Interest:**
 - *Primary:* Reduction in child's and parent's weight
 - *Secondary:* Quality of life, mood, coping with bullying, and cardiometabolic outcomes (i.e., blood pressure, lipids, and HbA1c)
- **Study Design:** Two-arm randomized controlled trial (RCT)
 - Sample Size: 1296 child-parent dyads (648 per arm)
- **Duration of Active Intervention:** 12 months
- **Length of Follow-up:** 18 months
- **Total Project Cost:** \$13.9M



Project 1: A Pragmatic Family Centered Approach to Childhood Obesity Treatment

- **Potential Impact:** Assists patients and primary care providers to choose the appropriate obesity treatment for the child. Also may inform clinicians and payers on effectiveness of two interventions that have different resource requirements
- **Patient-Centeredness:** Low-income and minority children could significantly benefit from obesity treatment completion. Study outcomes were endorsed by patients, parents, and other stakeholders
- **Engagement:** Four Advisory Boards of stakeholders will be involved in every phase of the project: 1) Family Advisory Board, 2) Evidence-Based Practice Advisory Board, 3) Provider Advisory Board, and 4) Payer Advisory Board. Dissemination efforts will leverage strong partnerships



Project 2: Comparison of Two- versus Three-Antibiotic Therapy for Pulmonary Mycobacterium Avium Complex Disease

- **Research Question:** Compare the effectiveness of a macrolide based multi-drug regimen containing two versus three antibiotics for pulmonary Mycobacterium avium complex (MAC)
- **Population:** Adult males and females with culture positive non-cavitary pulmonary MAC disease and no prior treatment for pulmonary MAC disease
- **Intervention:** Two drug antibiotic therapy (azithromycin and ethambutol)
- **Comparator(s):** Three drug antibiotic therapy (azithromycin, ethambutol, and rifampin)
- **Outcomes of Interest:**
 - *Primary:* Culture conversion at 12 months of treatment and tolerability of therapy
 - *Secondary:* Health-related quality of life, adverse event rates, and development of macrolide resistance
- **Study Design:** Multi-site randomized control trial
 - Sample Size: 500 patients
- **Duration of Active Intervention:** 12 months
- **Length of Follow-up:** 12 months
- **Total Project Cost:** \$6.2M



Project 2: Comparison of Two- versus Three-Antibiotic Therapy for Pulmonary Mycobacterium Avium Complex Disease

- **Potential Impact:** Provides the most definitive evidence on whether two-drug regimen is non-inferior to a three-drug regimen with respect to two consecutive negative cultures at 12 months and is superior with respect to tolerability
- **Patient-Centeredness:** Because the 2-drug regimen is expected to be better tolerated, this study will provide patients with new evidence about the potential benefits and harms of this treatment option
- **Engagement:**
 - The research question was developed as part of a PCORI Engagement Award
 - The study will utilize a Patient Advisory Panel consisting of 5 patient members. The study will also include a Study Advisory Committee comprised of patients, providers, representatives from patient advocacy groups, industry representatives, and a health system representative
 - The results will be disseminated to patients through partnerships with the advocacy and research organizations



Project 3: Integrated Physical and Mental Health Self-Management Compared to Chronic Disease Self-Management

- **Research Question:** What is the comparative effectiveness of I-IMR vs. CDSMP for improving patient self-management and health outcomes among individuals with Serious Mental Illness (SMI)?
- **Population:** Adults age 18+ with SMI diagnosis and a poorly-controlled chronic medical condition
- **Intervention:** Integrated-Illness Management Recovery (I-IMR)
- **Comparator(s):** Chronic Disease Self-Management Program (CDSMP)
- **Outcomes of Interest:**
 - *Primary:* Physical and mental self-management abilities, patient activation
 - *Secondary:* Physical and emotional health, ER use, and hospitalizations
- **Study Design:** RCT (mixed methods)
 - Sample Size: 600
- **Duration of Active Intervention:** I-IMR 16 weeks (1 hour/session) ; CDSMP 6 weeks (2.5 hours/session)
- **Length of Follow-up:** 12 months
- **Total Project Cost:** \$7.5M



Project 3: Integrated Physical and Mental Health Self-Management Compared to Chronic Disease Self-Management

- **Potential Impact:** Improving illness self-management skills for people living with serious mental illness and chronic conditions could improve their health and engagement in care. Study results could assist patients, providers, payers, and stakeholders in making better informed decisions about the effectiveness of illness self-management programs
- **Patient-Centeredness:** Addresses disparities in the morbidity of people with serious mental illness by comparing two available chronic disease self-management approaches, and is responsive to patients and stakeholders' interest in evaluating self-management programs that address both physical and mental wellbeing
- **Engagement:** The project's National Advisory Panel includes peer leaders, consumers, and family members. The Stakeholder Advisory Group includes peer support leaders, officials from the two states' departments of mental health, officials from the Medicaid health plan provider, and two national organizations focused on mental and behavioral health. The state and health plan officials and national mental and behavioral health organizations are committed to assisting with dissemination efforts



Project 4: Multi-Level Interventions for Increasing Tobacco Cessation at FQHCs

- **Research Question:** What is the impact of pragmatic and scalable interventions at both clinic and patient levels, that are designed to reduce tobacco use and reduce tobacco-related disparities?
- **Population:** People who smoke cigarettes currently, 18+ years of age, speak English or Spanish, and who present at participating Federally Qualified Health Center clinics
- **Interventions and Comparators:** Three-phase SMART trial design with four active interventions
- **Outcomes of Interest:**
 - *Primary:* Proportion of patients who enter Quitline treatment (Reach), smoking abstinence at 12 month follow-up (Efficacy), and Impact (Reach + Efficacy), health-related quality of life
 - *Secondary:* Process evaluation of implementation outcomes
- **Study Design:** Multi-level, three phase, sequential multiple assignment randomized trial
- **Sample Size:** 30 FQHC clinics; 6,000 participants
- **Duration of Active Intervention:** 6-12 months
- **Length of Follow-up:** 12 months
- **Total Project Cost:** \$9.8M



Project 4: Multi-Level Interventions for Increasing Tobacco Cessation at FQHCs

- **Potential Impact:** Increasing the reach and impact of tobacco Quitlines could dramatically reduce tobacco use prevalence at the population level and among low SES populations
- **Patient-Centeredness:** Patient-level interventions are sensitive to preferences of people who smoke; research is designed to help underserved people who smoke achieve goals of smoking abstinence by increasing opportunities to engage in evidence-based treatment; outcomes of abstinence and health-related QoL were identified through patient focus groups
- **Engagement:** Study Advisory Committee (SAC) composed of patient representatives, medical informatics and quitline experts, representatives from a statewide community health organization, statewide quitline, and participating FQHCs. A Patient Advisory Committee (PAC) also will be established for oversight of the study. SAC and PAC will be engaged during all phases of the research project. Two national organizations focused on community health and smoking cessation will assist with dissemination of study results



Project 5: KIDS FACE FEARS: Face-to-Face versus Computer-Enhanced Formats Pragmatic Study of Anxiety

- **Research Question:** What is the comparative effectiveness of face-to-face CBT vs online CBT for treating anxiety in children and adolescents in pediatric primary care?
- **Population:** Children ages 3-17 with mild-to-moderate anxiety in diverse primary care settings
- **Intervention:** Online CBT
- **Comparator(s):** Face-To-Face CBT
- **Outcomes of Interest:**
 - *Primary:* anxiety symptoms (parent and child report)
 - *Secondary:* child anxiety interference in life and parental depression, anxiety, and stress
- **Study Design:** 2-arm randomized clinical trial
 - Sample Size: 1856
- **Duration of Active Intervention:** 12 weeks
- **Length of Follow-up:** 2 years
- **Total Project Cost:** \$13.6M



Project 5: KIDS FACE FEARS: Face-to-Face versus Computer-Enhanced Formats Pragmatic Study of Anxiety

- **Potential Impact:** Addresses a PCORI-designated special area of emphasis topic on comparing digital applications of CBT to an active control (e.g. face-to-face CBT) for the treatment of anxiety in children and adolescents
- **Patient-Centeredness:** Focuses on outcomes of interest to patients and parents
- **Engagement:** Parents played a large role in study design. Groups engaged include the family advisory council at 2 medical centers and a Latino parent research committee at one of the site institutions



Cycle 2 2017 – Pragmatic Clinical Studies

*5 Recommended Projects**

PFA	Amount Budgeted	Proposed Total Award
Cycle 2 2017 Pragmatic Clinical Studies	\$52 Million	\$51 Million

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Board Vote

Call for a Motion to:

- **Approve** funding for the recommended slate of awards from the Cycle 2 2017 Pragmatic Clinical Studies PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Symptom Management for Patients with Advanced Illness

Cycle 2 2017 Award Slate

Christine Goertz, DC, PhD

Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH

Chief Science Officer



Cycle 2 2017 – Symptom Management for Patients with Advanced Illness

Objective of the PFA

- Fund studies examining long-term outcomes (≥ 6 months) for the comparison of evidence-based pharmacological treatments vs. other management strategies for symptoms experienced by patients with advanced illness and a life expectancy of greater than six months

Priority Research Question:

- Based on patient- and caregiver-centered outcomes, what is the comparative clinical effectiveness of two or more approaches (including at least one pharmacological intervention) on symptom management in patients living with advanced illness, for one or more of the following symptoms?
 - Pain
 - Fatigue
 - Dyspnea
 - Anorexia/cachexia
 - Nausea/vomiting
 - Depression and/or anxiety



Cycle 2 2017 – Symptom Management for Patients with Advanced Illness

Merit Review Criteria

1. Potential for the study to fill critical gaps in evidence
2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
3. Scientific merit (research design, analysis, and outcomes)
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder engagement



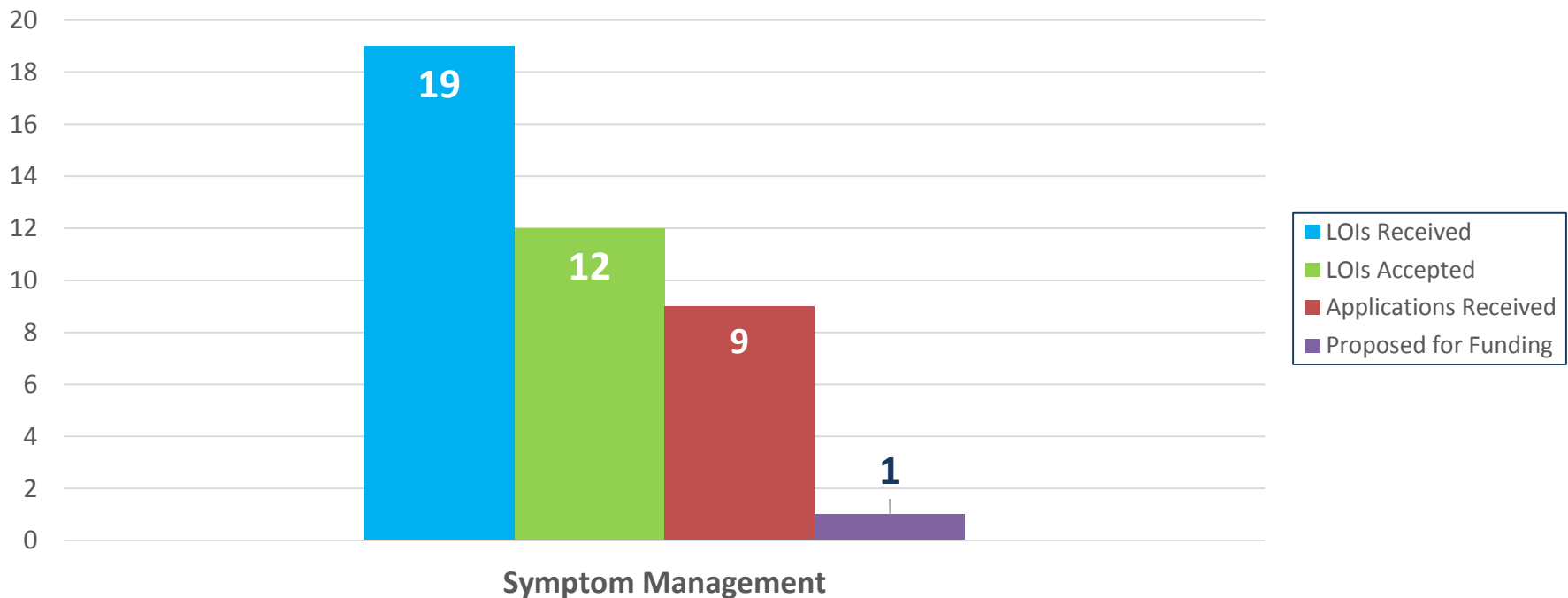
Cycle 2 2017 – Symptom Management for Patients with Advanced Illness

Process Overview

- 19 Letters of Intent (LOIs) submitted
- 12 LOIs invited to submit a full application (**63%**)
- 9 applications were received (**75% of invited LOIs**)

Funding rate is 11 percent

- We are proposing to fund 1 application* out of 9 received applications



Cycle 2 2017 – Symptom Management for Patients with Advanced Illness

*1 Recommended Project**

Project
Personalized Treatments for Advanced Medical Illness Patients with Depression (\$2.6M)

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Project 1: Personalized Treatments for Advanced Medical Illness Patients with Depression

- **Research Question:** What is the comparative effectiveness of 3 treatment strategies for depressive symptoms in patients with advanced heart failure?
- **Population:** Inpatients with a diagnosis of advanced heart failure (AHF) who screen positive for depression
- **Intervention** Behavioral Activation (BA), Combined BA + MEDS
- **Comparator(s):** Antidepressant medication (MEDS)
- **Outcomes of Interest:**
 - *Primary:* Change in self-reported depressive symptom severity, as measured by PHQ-9
 - *Secondary:* Functioning, HRQoL, global health, caregiver burden, ED visits, hospital readmission, total days in the hospital, mortality
- **Study Design:** 3-arm, single site RCT, sample size=450
- **Duration of Active Intervention:** 6 months
- **Length of Follow-up:** 12 months
- **Total Project Cost:** \$2.6M



Project 1: Personalized Treatments for Advanced Medical Illness Patients with Depression

- **Potential Impact:**
 - Compares long-term benefits and harms for psychotherapeutic and pharmacologic interventions
 - BA is easily implemented, and therefore, a broader range of providers may be able to deliver this psychotherapeutic approach
- **Patient-Centeredness:**
 - Evaluates full range of long-term (1-year) patient and caregiver outcomes
- **Engagement:**
 - Two patients with heart failure and depression helped to develop proposal
 - Engagement plan well-developed with clear roles and responsibilities
 - Professional organizations will be involved in dissemination



Cycle 2 2017 – Symptom Management for Patients with Advanced Illness

*1 Recommended Project**

PFA	Amount Budgeted	Proposed Total Award
Symptom Management for Patients with Advanced Illness	\$21 Million	\$2.6 Million

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Board Vote

Call for a Motion to:

- **Approve** funding for the recommended slate of awards from the Cycle 2 2017 Symptom Management for Patients with Advanced Illness PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Medication-Assisted Treatment (MAT) Delivery for Pregnant Women with Substance Use Disorders Involving Prescription Opioids and/or Heroin

Cycle 2 2017 Award Slate

Christine Goertz, DC, PhD

Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH

Chief Science Officer



Cycle 2 2017 – MAT Delivery for Pregnant Women with OUD

Objective of the PFA

- This PFA supports patient-centered CER on the delivery of Medication-Assisted Treatment (MAT) for pregnant women with Opioid Use Disorder (OUD)
- Study design: Large RCTs or well-justified observational studies
 - Delivery models or their components must have evidence of efficacy or be in common use and should be well characterized to facilitate replication and dissemination efforts

Priority Research Questions:

- What is the comparative effectiveness of alternative models for comprehensive OUD treatment delivery on maternal and neonatal outcomes in pregnant and post-partum women with different levels of addiction severity?
- What is the comparative effectiveness of remotely supported OUD treatment delivery to pregnant women that includes more versus less resource-intense approaches to induction and psychosocial support for office-based opioid treatment, in terms of maternal and neonatal outcomes?



Cycle 2 2017 – MAT Delivery for Pregnant Women with OUD

Merit Review Criteria

1. Potential for the study to fill critical gaps in evidence
2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
3. Scientific merit (research design, analysis, and outcomes)
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder engagement



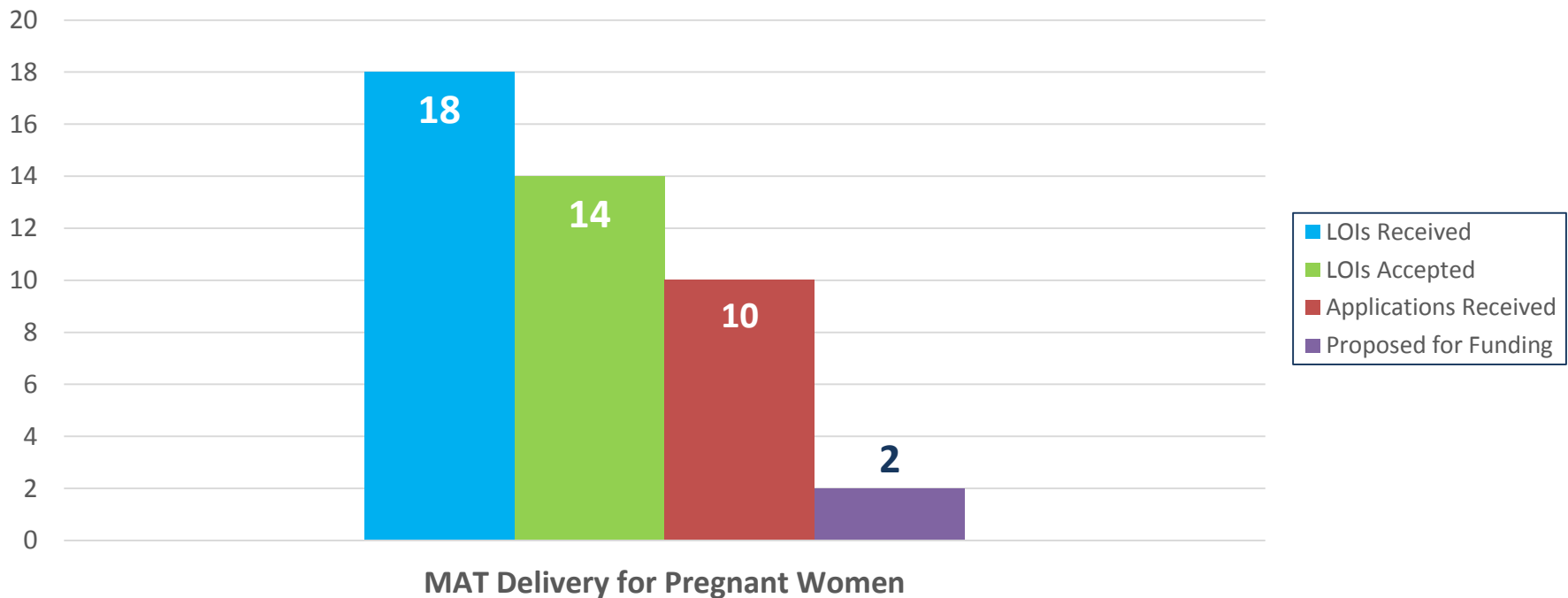
Cycle 2 2017 – MAT Delivery for Pregnant Women with OUD

Process Overview

- 18 Letters of Intent (LOIs) submitted
- 14 LOIs invited to submit a full application (**78%**)
- 10 applications were received (**71% of invited LOIs**)

Funding rate is 20 percent

- We are proposing to fund 2 applications* out of 10 received applications



Cycle 2 2017 – MAT Delivery for Pregnant Women with OUD

*2 Recommended Projects**

Project
Moms in Recovery (MORE): Defining Optimal Care for Pregnant Women and Infants (\$5.3M)
PATHways: Comparative Effectiveness Study of Peripartum Opioid Use Disorder in Rural Kentucky (\$4.9M)

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Project 1: Moms in Recovery (MORE): Defining Optimal Care for Pregnant Women and Infants

- **Research Question:** What is the comparative effectiveness of integrated vs referral-based MAT delivery models for pregnant women with OUD and their infants for maternal and infant outcomes?
- **Population:** Pregnant women with OUD receiving prenatal care and MAT
- **Comparators:**
 - Integrated Care (prenatal care and MAT provided by a team of clinicians in one setting);
 - Referral-based care (prenatal care at obstetric practice and referral to MAT)
- **Outcomes of Interest:**
 - *Primary:* Illicit opioid use; treatment retention; perinatal complications
 - *Secondary:* Neonatal Abstinence Syndrome; retention of custody; quality of life
- **Study Design:** Prospective observational mixed-methods design
 - Sample Size: 2,000
- **Duration of Active Intervention:** 2- 10.5 months, depending on the week of the pregnancy at enrollment into care; data collection 3rd trimester through 6 months post-partum
- **Length of Follow-up:** 6 months post-partum
- **Total Project Cost:** \$5.3M



Project 1: Moms in Recovery (MORE): Defining Optimal Care for Pregnant Women and Infants

- **Potential Impact:** The study will provide important information to obstetric practices, patients, and providers about two existing OUD treatment delivery models. The inclusion of maternal and infant outcomes allows for a careful assessment of these options for specific subgroups based on their characteristics
- **Patient-Centeredness:** Providing evidence to help determine the optimal delivery of MAT for pregnant women is patient-centered. The study includes patient-reported outcomes and qualitative patient interviews regarding patient experience of care that will help inform decisions about care delivery. Postpartum women receiving MAT were interviewed to inform research question and study outcomes
- **Engagement:** A large network of maternity care providers throughout the study target region, an advocacy organization for pediatric providers, and a drug abuse and addiction research collaborative are stakeholders in this study. Patients and stakeholder partners have been and will be collaborators in all phases of the study, including dissemination efforts



Project 2: PATHways: Comparative Effectiveness Study of Peripartum Opioid Use Disorder in Rural Kentucky

- **Research Question:** What is the comparative effectiveness of alternative models for comprehensive OUD treatment delivery to rural pregnant women for maternal and neonatal outcomes?
- **Population:** Pregnant women with OUD at 6 to 32 weeks gestation who are obtaining prenatal care at rural study sites and receiving MAT
- **Comparators:**
 - Telemedicine consultations with clinicians with expertise in substance abuse counseling, Maternal Fetal Medicine, Addiction Medicine, and Neonatology;
 - In-person group sessions with a Perinatal Nurse Facilitator and Peer Support Specialist
- **Outcomes of Interest:**
 - *Primary:* Rate of treatment-requiring Neonatal Abstinence Syndrome (NAS)
 - *Secondary:* Custody status, smoking cessation, relapse rate, maternal depression, infant developmental milestones
- **Study Design:** Cluster RCT
 - Sample Size: 1,620 patients; 12 sites (135 patients per site)
- **Duration of Active Intervention:** 8 to 13 months, depending on week of pregnancy at enrollment
- **Length of Follow-up:** 6 months post-partum
- **Total Project Cost:** \$4.9M



Project 2: PATHways: Comparative Effectiveness Study of Peripartum Opioid Use Disorder in Rural Kentucky

- **Potential Impact:** The study results will provide important information to obstetric practices and providers serving rural populations about delivery of comprehensive OUD treatment, and to patients about which option to choose. The inclusion of maternal and infant outcomes and follow up until 6 months post-partum will allow for a careful assessment of these options for specific subgroups based on their characteristics
- **Patient-Centeredness:** Comparing comprehensive OUD treatment delivery for pregnant women and their infants in rural areas, and the primary outcome (rate of NAS) are patient-centered. The comparators were selected based on focus groups and direct interviews with patients. Patients will be involved throughout the conduct of the study
- **Engagement:** The study will utilize a Study Advisory Committee consisting of state government agency representatives, a community action group, clinicians, payer, and patient partners. National stakeholders include a nonprofit organization of women's health care physicians, an advocacy organization for maternal-fetal medicine, and a nonprofit membership organization for pregnant and nursing women. SAC members will be involved throughout the study, including in dissemination efforts



Cycle 2 2017 – MAT Delivery for Pregnant Women with OUD

*2 Recommended Projects**

PFA	Amount Budgeted	Proposed Total Award
MAT Delivery for Pregnant Women with Substance Use Disorders Involving Prescription Opioids and/or Heroin	\$14 Million	\$10.2 Million

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Board Vote

Call for a Motion to:

- **Approve** funding for the recommended slate of awards from the Cycle 2 2017 Medication-Assisted Treatment Delivery for Pregnant Women with Substance Use Disorders PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Optimized Multidisciplinary Treatment Programs for Nonspecific Chronic Low Back Pain Cycle 1 2017 Award Slate

Christine Goertz, DC, PhD

Chair, Selection Committee

Evelyn Whitlock, MD, MPH

Chief Science Officer



Cycle 1 2017 – Treatment Programs for Nonspecific Chronic Low Back Pain

Objective of the PFA

- PCORI seeks to fund large, randomized controlled trials or well-justified observational studies that compare the effectiveness of optimized, multidisciplinary nonsurgical treatment programs involving combined or sequenced interventions for patients with nonspecific chronic low back pain (LBP)
- Treatment programs must be evidence-based and are expected to be well-characterized to facilitate replication and dissemination efforts

Priority Research Question:

- What is the comparative clinical effectiveness of optimized, multidisciplinary nonsurgical treatment programs involving combined or sequenced interventions for patients with nonspecific chronic low back pain?



Cycle 1 2017 – Treatment Programs for Nonspecific Chronic Low Back Pain

Merit Review Criteria

1. Potential for the study to fill critical gaps in evidence
2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
3. Scientific merit (research design, analysis, and outcomes)
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder engagement



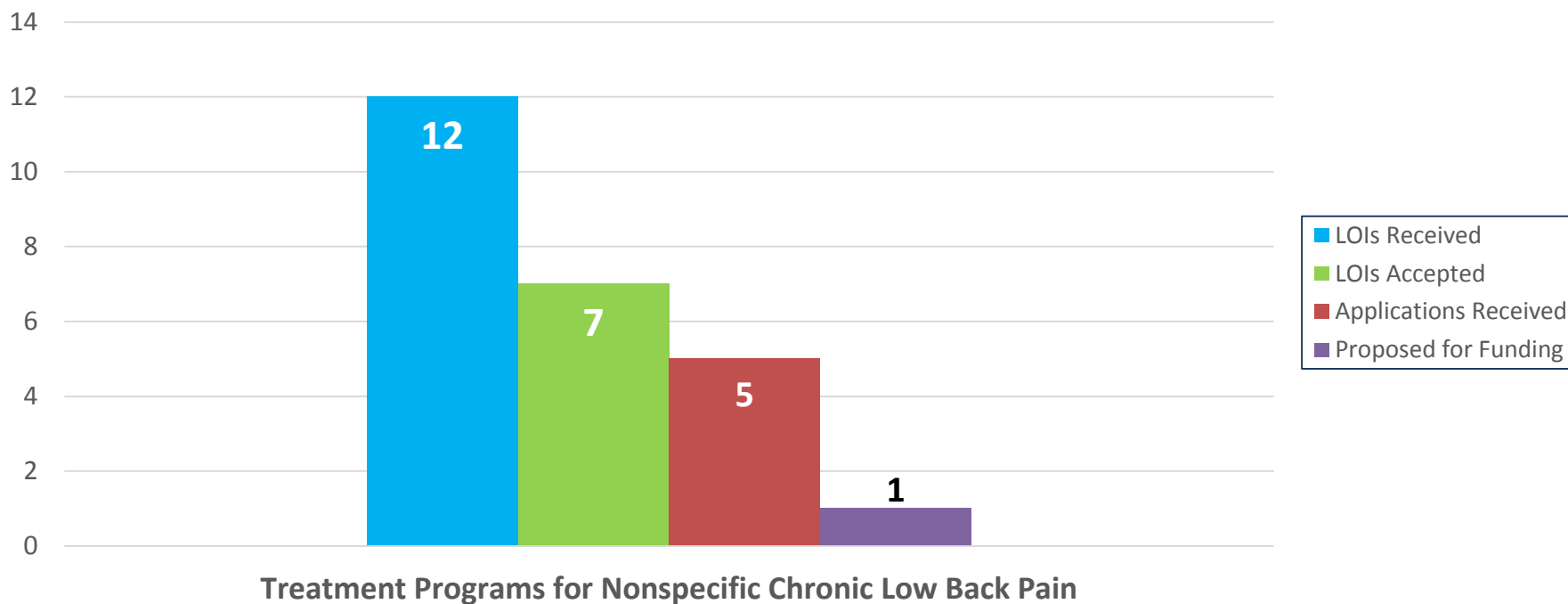
Cycle 1 2017 – Treatment Programs for Nonspecific Chronic Low Back Pain

Process Overview

- 12 Letters of Intent (LOIs) submitted
- 7 LOIs invited to submit a full application (58%)
- 5 applications were received (71% of invited LOIs)

Funding rate is 20 percent

- We are proposing to fund 1 application* out of 5 received applications



Cycle 1 2017 – Treatment Programs for Nonspecific Chronic Low Back Pain

*1 Recommended Project **

Project
Optimizing Treatment Sequencing for Patients with Chronic, Non-Specific Low Back Pain (\$9.7M)

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Project 1: Optimizing Treatment Sequencing for Patients with Chronic, Non-Specific Low Back Pain

- **Research Questions:**
 - What is the comparative effectiveness of physical therapy (PT) vs. cognitive behavioral therapy (CBT) as initial treatments for patients with chronic low back pain (LBP)?
 - For non-responders, does switching treatments improve response?
- **Study Design:** SMART RCT with sample size 945 from 3 study sites
- **Phase I interventions:** PT vs. CBT
- **Phase II interventions (if non-response after 10 weeks)**
 - Mindfulness-based intervention vs. other initial treatment option (CBT or PT)
- **Population:** 18-65 y with chronic LBP
 - No spine surgery in last 12 months
 - Oswestry score > 24% and average pain rating > 4
- **Outcomes (through 12 months):**
 - Primary: pain intensity and function
 - Secondary: PROMIS-29 dimensions (anxiety, depression, fatigue, sleep, social role function, pain interference), healthcare utilization, long-term opioid use for back pain
- **Total Project Costs:** \$9.7M



Project 1: Optimizing Treatment Sequencing for Patients with Chronic, Non-Specific Low Back Pain

- **Potential Impact:** The impact of different sequences of the various evidence-based treatments proposed has not been evaluated in prior research. The research findings would have potential to fill existing gaps in the literature
- **Patient-Centeredness:** Patients and other end-use stakeholders contributed to the study design, which addresses challenges brought forward by patients and uses patient-centered outcomes, including multiple dimensions of quality of life
- **Engagement:** The investigative team, well-experienced in orthopedic rehabilitation and trauma, have identified a multi-pronged approach in partnership with patients and leading pain management stakeholders to disseminate study information and facilitate implementation into practice



Cycle 1 2017 – Treatment Programs for Nonspecific Chronic Low Back Pain

*1 Recommended Project **

PFA	Amount Budgeted	Proposed Total Award
Optimized Multidisciplinary Treatment Programs for Nonspecific Chronic Low Back Pain	\$43 Million	\$9.7 Million

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Board Vote

Call for a Motion to:

- **Approve** funding for the recommended slate of awards from the Cycle 1 2017 Optimized Multidisciplinary Treatment Programs for Nonspecific Chronic Low Back Pain PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Break

We will return at 3:15 pm ET



Join the conversation on Twitter via
@PCORI



Targeted PFA: Psychosocial Interventions with Office-Based Opioid Treatment (OBOT) for Opioid Use Disorder

Robert Zwolak, MD, PhD

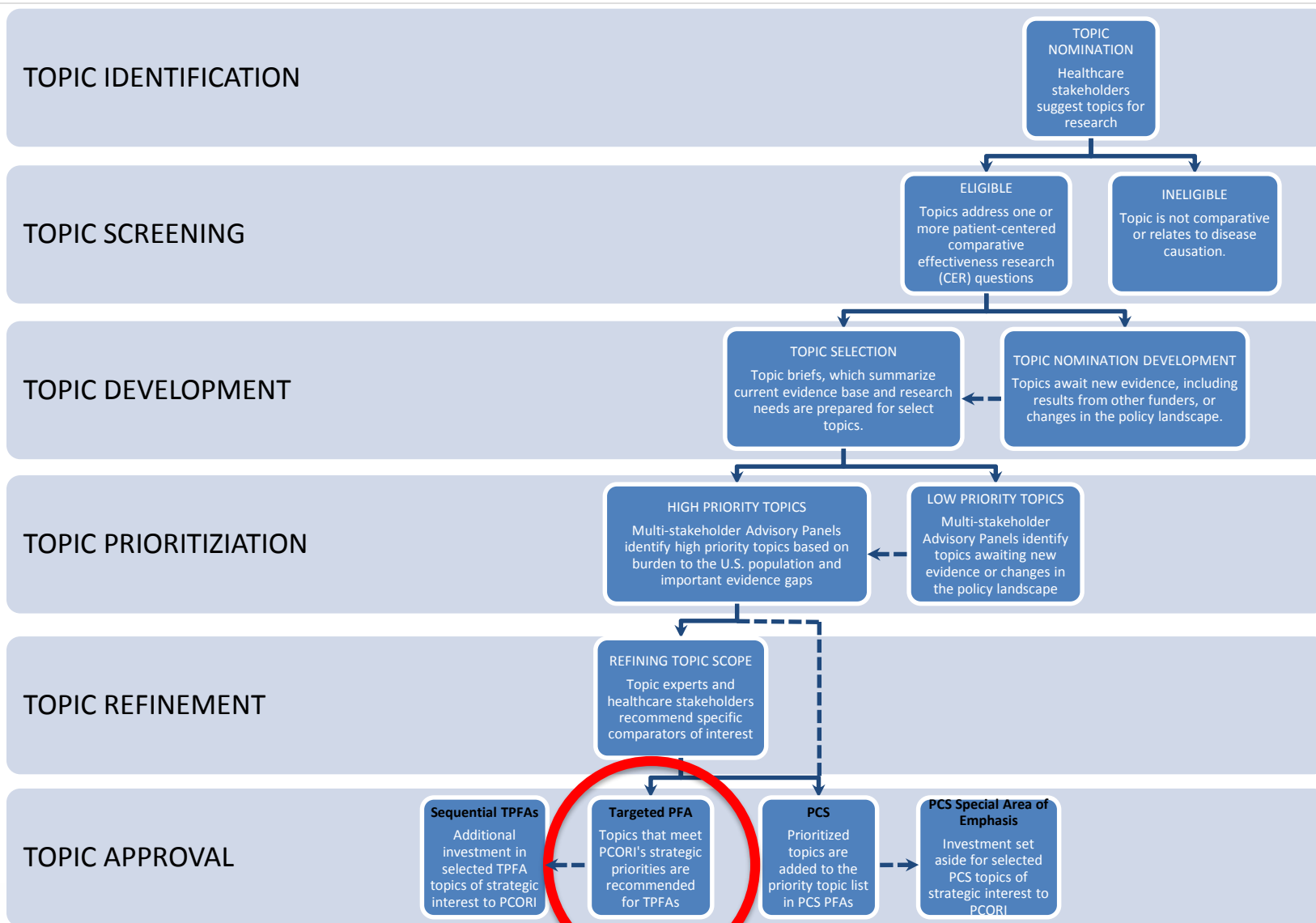
Chair, Science Oversight Committee

Evelyn P. Whitlock, MD, MPH

Chief Science Officer



PCORI Topic Prioritization Pathway



Psychosocial Interventions with Office-Based Opioid Treatment (OBOT) for Opioid Use Disorder

- Medication-assisted treatment (MAT) is the **first-line evidence-based treatment** for opioid use disorder (OUD)
- **Buprenorphine** can be offered in primary care settings (OBOT) and prescribed by MDs, PAs, NPs, has a favorable safety profile, and is now available in long-acting form = **potential for expanded access to MAT**
- Federal law requires clinicians prescribing MAT to either provide or refer patients to **adequate psychosocial services**
- National guidelines recommend evidence-based psychosocial services as part of OBOT, but **do not indicate which services are better for which populations**
- Individual trials and systematic reviews show **mixed results** on which psychosocial treatments are (most) effective
- There is **limited evidence** indicating which psychosocial services are most effective with buprenorphine specifically
- **Stakeholders strongly support the production of better evidence** to inform the provision of MAT, and the expansion of access to MAT



Psychosocial Interventions with Office-Based Opioid Treatment (OBOT) for Opioid Use Disorder

Question of interest: What is the comparative effectiveness of psychosocial interventions versus standard medical management for patients who receive office-based opioid treatment (OBOT) with buprenorphine? *Which psychosocial interventions are most effective, and for whom?*

- **Populations:** Could include adolescents, patients with multiple comorbidities, ethnic and racial minorities
- **Interventions/comparators:** Standard medical management (SMM), individual or group addiction counseling, cognitive behavioral therapy (CBT), contingency management (CM), family therapy, self-help groups, 12-step-oriented treatments, community reinforcement approach (CRA)
 - *Approaches must be evidence-based, protocolized, and reproducible*
- **Outcomes:** Illicit opioid use, treatment adherence/retention, patient function, ED visits, overdose, provider satisfaction
- **Timing:** At least 1 year of follow-up
- **Setting:** Outpatient clinics/practices where OBOT is offered



Requested Research Commitment

- **Total commitment requested for this Targeted PFA is up to \$25M in total costs**
 - Estimated number of studies: 4-5
 - Total direct cost per study: \$4M
 - Maximum project duration: 4 years



Timeline

Action	Date
SOC Approval	April 19, 2018
Board of Governors Vote	April 30, 2018
Preannouncement Released	May 2, 2018
Targeted PFA Announced	June 1, 2018
Letter of Intent Due	June 28, 2018
Application Deadline	September 25, 2018
Merit Review	December 2018
Board Approval/Awards Announced	April 2019



Board Vote

Call for a Motion to:

- **Approve** the development of and release of the Psychosocial Interventions with Office-Based Opioid Treatment (OBOT) for Opioid Use Disorder PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



PCORnet Update

Joe Selby, MD, MPH

Executive Director, PCORI

Adrian Hernandez, MD, MHS

Duke Clinical Research Institute

Keith Marsolo, PhD

Cincinnati Children's Hospital Medical Center



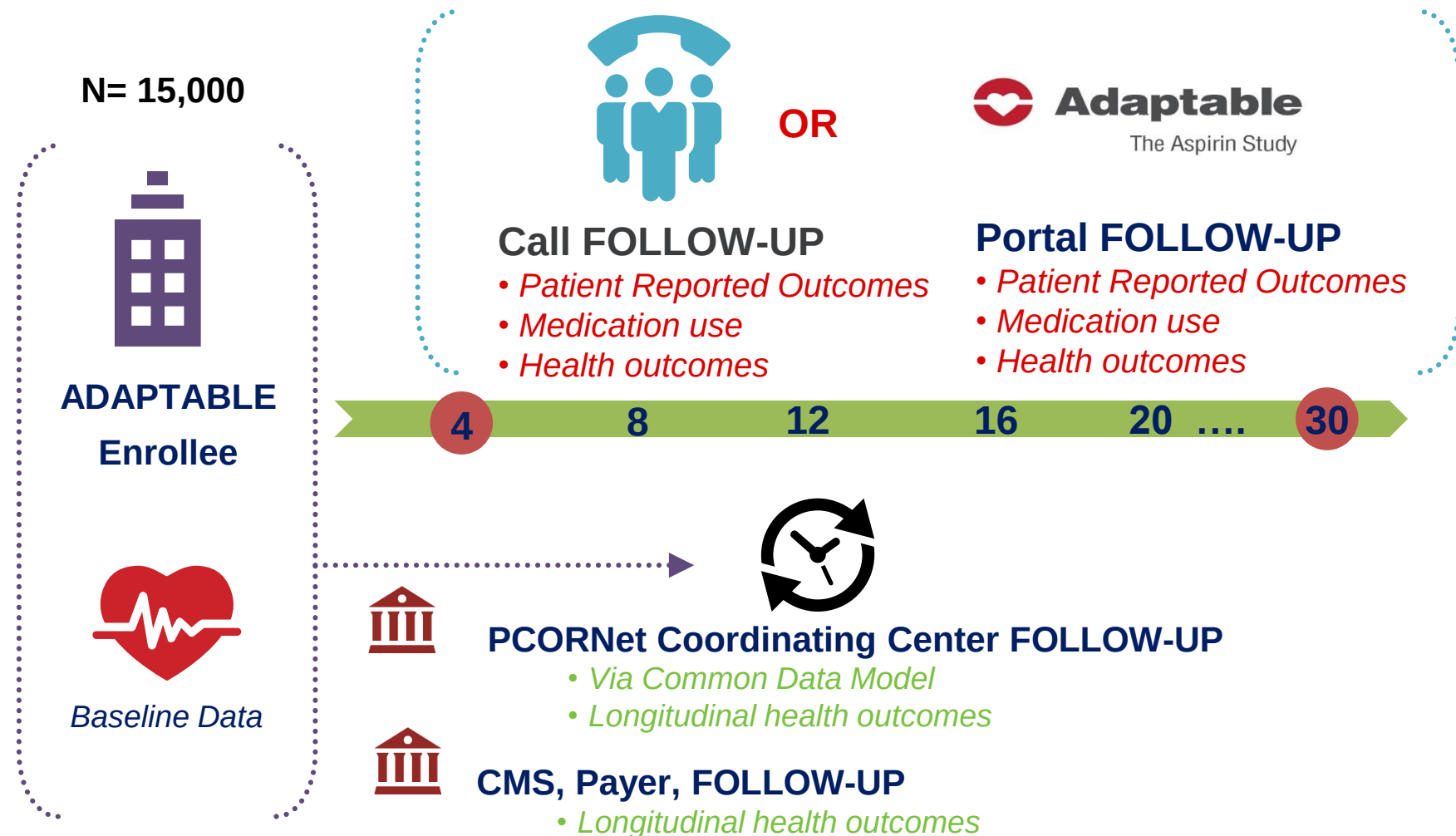
ADAPTABLE: Participant Identification and Recruitment

Adrian Hernandez, MD, MHS

Duke Clinical Research Institute

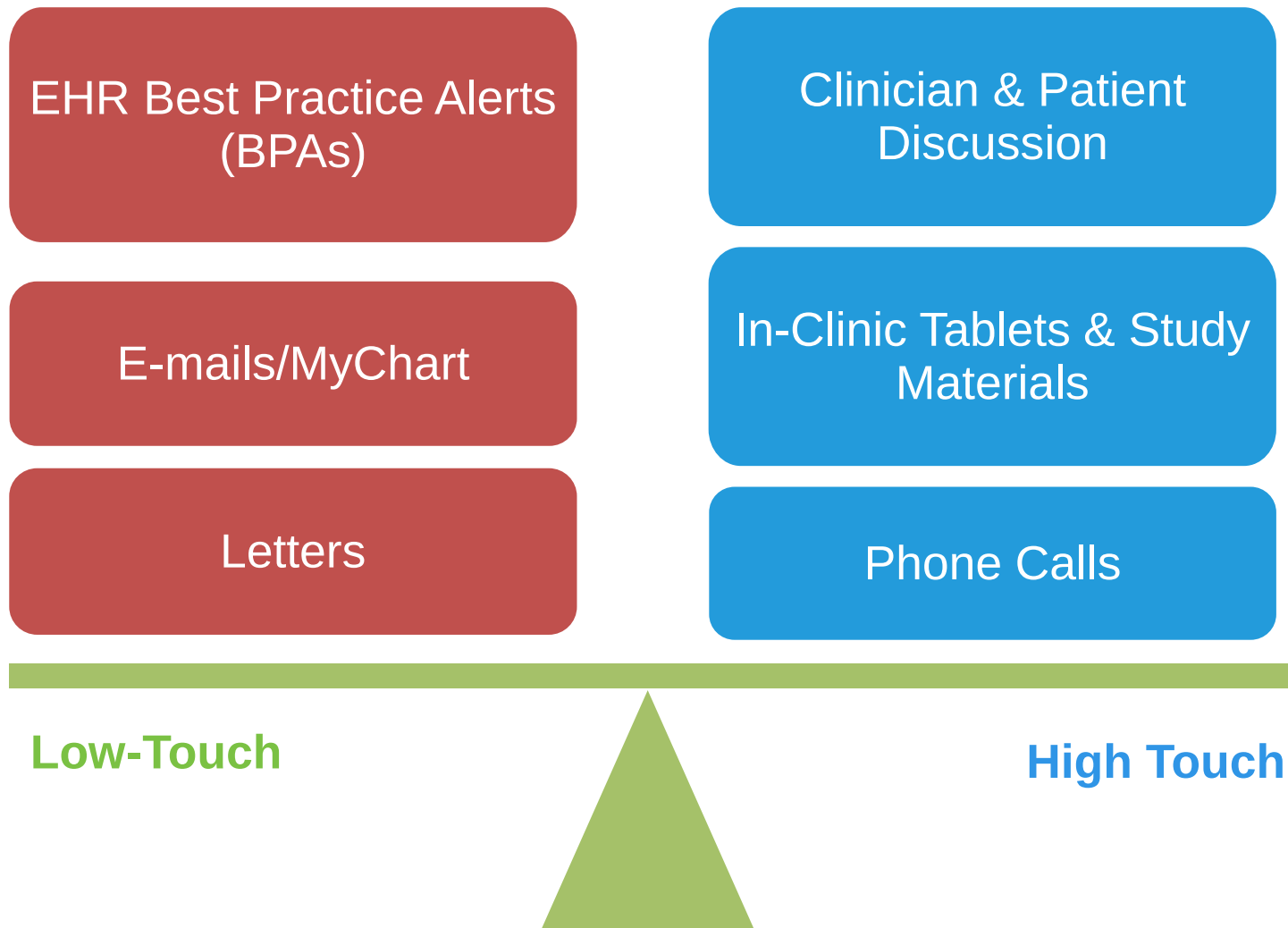


Enabling Pragmatic Research: eScreening, eEnrollment and eFollow-up

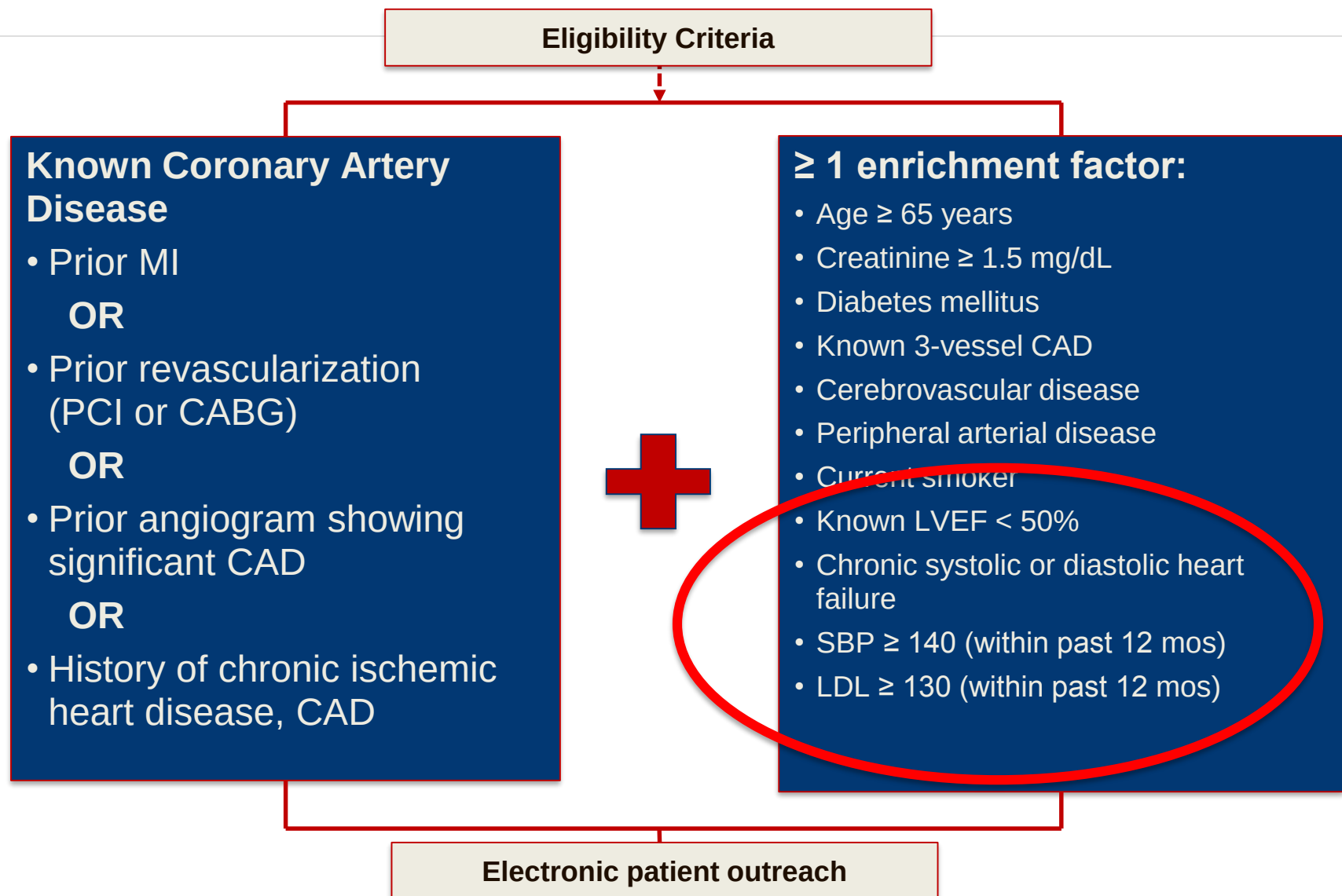


Recruitment Methods

(Multi-Modal, Multi-Touch Strategy)



Adapting to a Computable Phenotype



Improving the Computable Phenotype ...and Enrollment

- Optimization of Eligibility Criteria Eligibility Criteria with EHR data
 - Align with data availability in local datamarts
 - Maximize eligible pool without losing specificity
- Optimization of Base Code
 - Refine CP at select sites prior to distribution to all participating sites
- Review Implementation of Local Filters
 - Evaluate impact of filters on eligible pool on a site by site basis
 - Coordinating Center central review and engagement with each site to facilitate removal of local CP filters impacting eligible pool of participants
- Refresh Quarterly to Identify Newly Eligible Patients



How do you participate? Get a Golden Ticket

 **Adaptable**
The Aspirin Study

En Español

Let's get started!

Thank you for taking the time to find out more details about the ADAPTABLE aspirin study.
With your help, we hope to find out what is the right dose of aspirin for people with heart disease.

Got a code?

Please enter in the special code that was included in your invitation:

ENTER

No code? No problem!

You can still learn more about this study even if you have not been asked to participate.



CONTINUE

Already have a profile? [Login](#)



The Participant Portal

The screenshot shows the 'Adaptable The Aspirin Study' participant portal. At the top is a blue header with the Adaptable logo and text size controls. Below the header, a central message states 'There are 5 steps to join the study!' and provides an estimate of time per step. Five cards represent the steps: Watch (5 min), Read (15 min), Answer (5 min), Join (3 min), and Inform (5 min). Each card includes an icon and a brief description. At the bottom, there is a cartoon character of a woman and a large green 'LET'S GET STARTED' button.

Adaptable
The Aspirin Study

TEXT SIZE

There are 5 steps to join the study!

The time on each card is an estimate of how long it will take you to complete each section.
There are no time limits, so please go at your own pace.

Step	Icon	Action	Description	Time
1	Play button	Watch	the ADAPTABLE short video	5 min
2	Glasses	Read	more details about participating in ADAPTABLE	15 min
3	Form with checkmark	Answer	a few questions about the study	5 min
4	Signature	Join	the ADAPTABLE study	3 min
5	Medical bag	Inform	us about your current health	5 min

LET'S GET STARTED



pcornet

POWERED BY



Contact Us Help
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adaptablepatient.com



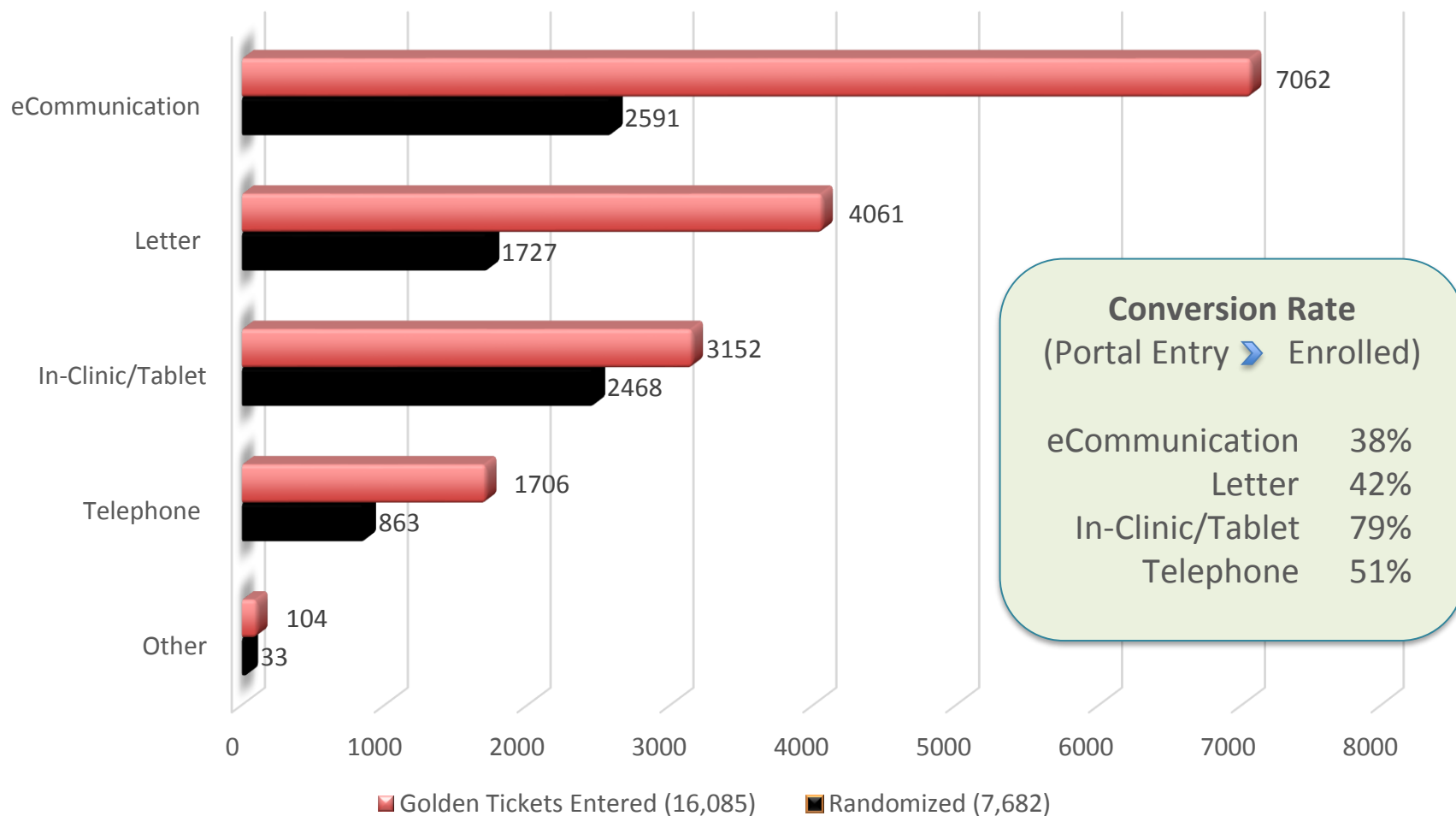
Phased Recruitment Strategy

(200-500 patients approached per week)

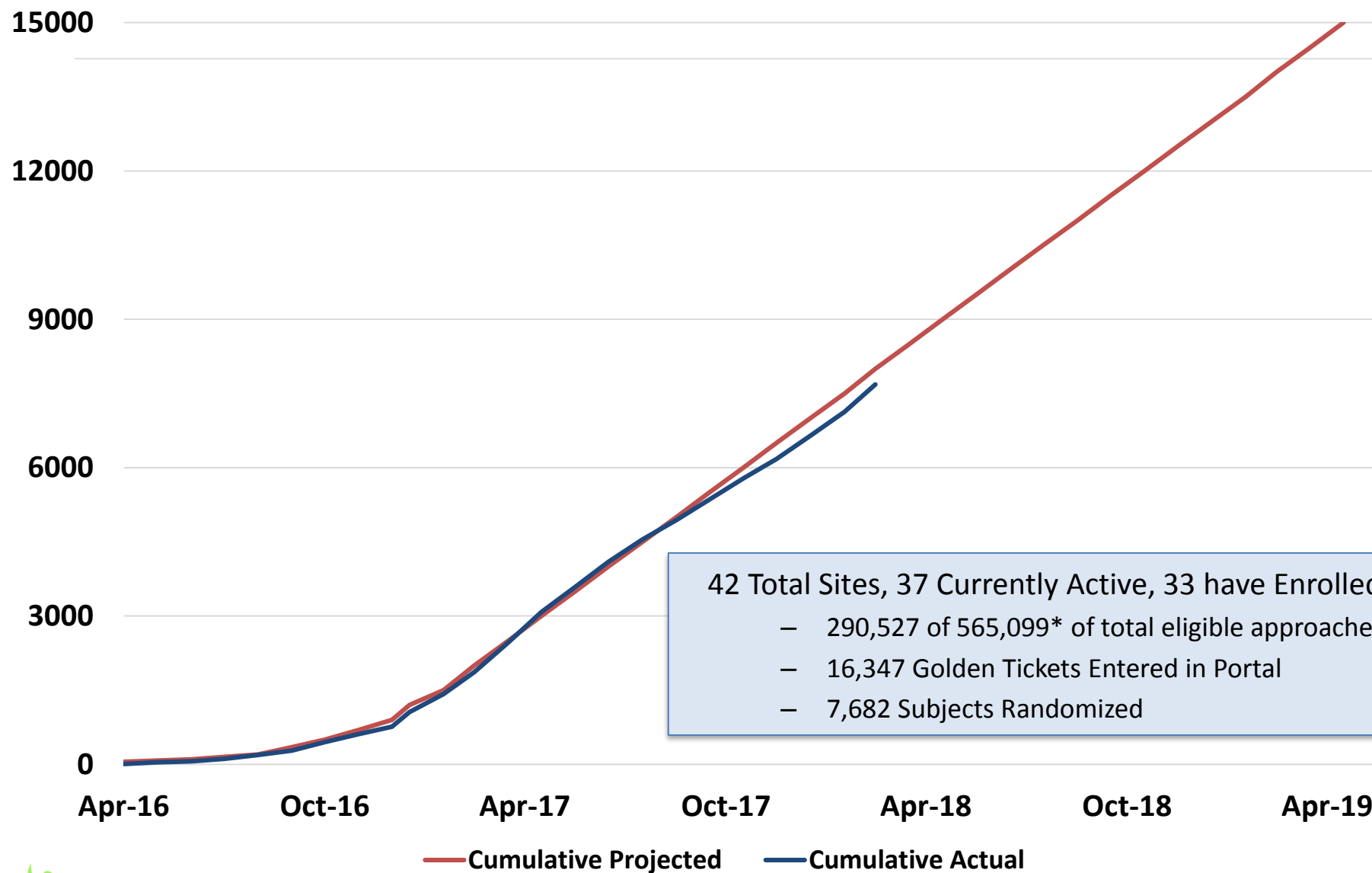
Monday	Tuesday	Wednesday
Week 1	Initial email script 1 – Group 1	
Week 2 Remove declines, ineligible deceased	Initial email script 1 – Group 2 Follow up email script - Group 1	Phone follow up Group 1 initial
Week 3 Remove declines, ineligible deceased	Follow up email script - Group 2	Phone follow up Group 2 Initial
Week 4 Remove declines, ineligible deceased	Final email script – Group 1	Phone follow up Group 1 final
Week 5 Remove declines, ineligible deceased	Final email script – Group 2 Initial email - Group 3	Phone follow up Group 2 final



Invitation Methods: Entered Portal vs Enrolled



ADAPTABLE Enrollment Curve



A Learning Network

Number of Sites, Total Approached, and Enrolled Increased Over Last 2 Years with Improved Efficiency

2016

Site	Apr 2016	May 2016	Jun 2016	Jul 2016	Aug 2016	Sep 2016	Oct 2016	Nov 2016	Dec 2016
Total Enrolled	8	32	22	50	77	90	171	163	151
# of Sites Approaching	2	2	2	2	4	6	10	14	16
Total Approached	126	381	380	1,196	1,920	2,342	7,499	4,160	7,299

2017

Site	Jan 2017	Feb 2017	Mar 2017	Apr 2017	May 2017	Jun 2017	Jul 2017	Aug 2017	Sep 2017	Oct 2017	Nov 2017	Dec 2017
Total Enrolled	294	362	448	600	509	512	503	456	395	414	426	391
# of Sites Approaching	17	22	21	26	26	27	27	28	28	28	29	30
Total Approached	4,455	9,813	12,857	14,105	16,435	14,486	11,592	5,249	5,092	1,971	139,325*	3,911

2018

Site	Jan 2018	Feb 2018	Mar 2018
Total Enrolled	475	480	553
# of Sites Approaching	30	32	32
Total Approached	4,743	9,569	8,785

*Increase in total approached due to HealthCore



Retention and Follow-up

CDRN	%WDC	% Limited Participation
1	2.4%	0.6%
2	4.4%	0.9%
3	1.0%	1.3%
4	2.6%	0.0%
5	1.1%	1.0%
6	2.5%	0.6%
7	1.9%	0.3%
8	2.9%	0.2%
9	1.3%	0.0%
10	1.0%	1.6%
Total	1.7%	0.9%

- **Withdrawal of consent varies by site**
- **Decreasing over time**
- **Most common reasons reported for changing participation level:**
 - #1 Medication/Health Issues
 - #2 Privacy Concerns



What Have We Learned from Adaptable?

Successes

ADAPTORS!

National, professional societies

E-Identification of ~ 400,000

E-approach of ten's of thousands

Challenges

Varied clinical and patient engagement across centers/sites

Lack of integration of clinical, trial personnel and informatics teams

Institutional policies, procedures and barriers: Patient preferences for research; ability to approach patients; local dogma

Lessons Learned

Continue:

- Continue ADAPTORS model
- Professional societies
- E-Identification and e-approach
- Multi-touch approach

Improve for Future Studies:

- Engagement (Local to National to Local Combination)
- Test different engagement models
- Understand patient preferences for research and potential participants
- Include multi-touch approaches
- Increase return of value to participants
- CHANGE institutional policies
- PRIORITIZE PCORnet



Querying in PCORnet

Keith Marsolo, PhD

Cincinnati Children's Hospital Medical Center

Presenting on behalf of the PCORnet Coordinating Center's
Distributed Research Network Operations Center (DRN OC)



Overview

- The PCORnet Coordinating Center was asked to provide a response to the PCORI Board's request for a searchable tool in the public domain to inform study feasibility and provide information on conditions of interest
- This presentation provides background on PCORnet's current query capabilities & describes potential options for the future



PCORnet Data Strategy – Enabling distributed research at a national scale

- Standardize data into a common data model (CDM)
- Focus on data quality – data curation
- Operate a secure distributed query infrastructure
 - Develop *re-usable, parameterized tools* to query the data
 - Send questions to the data and only return required information
- Iterative cycle of learning and improvement

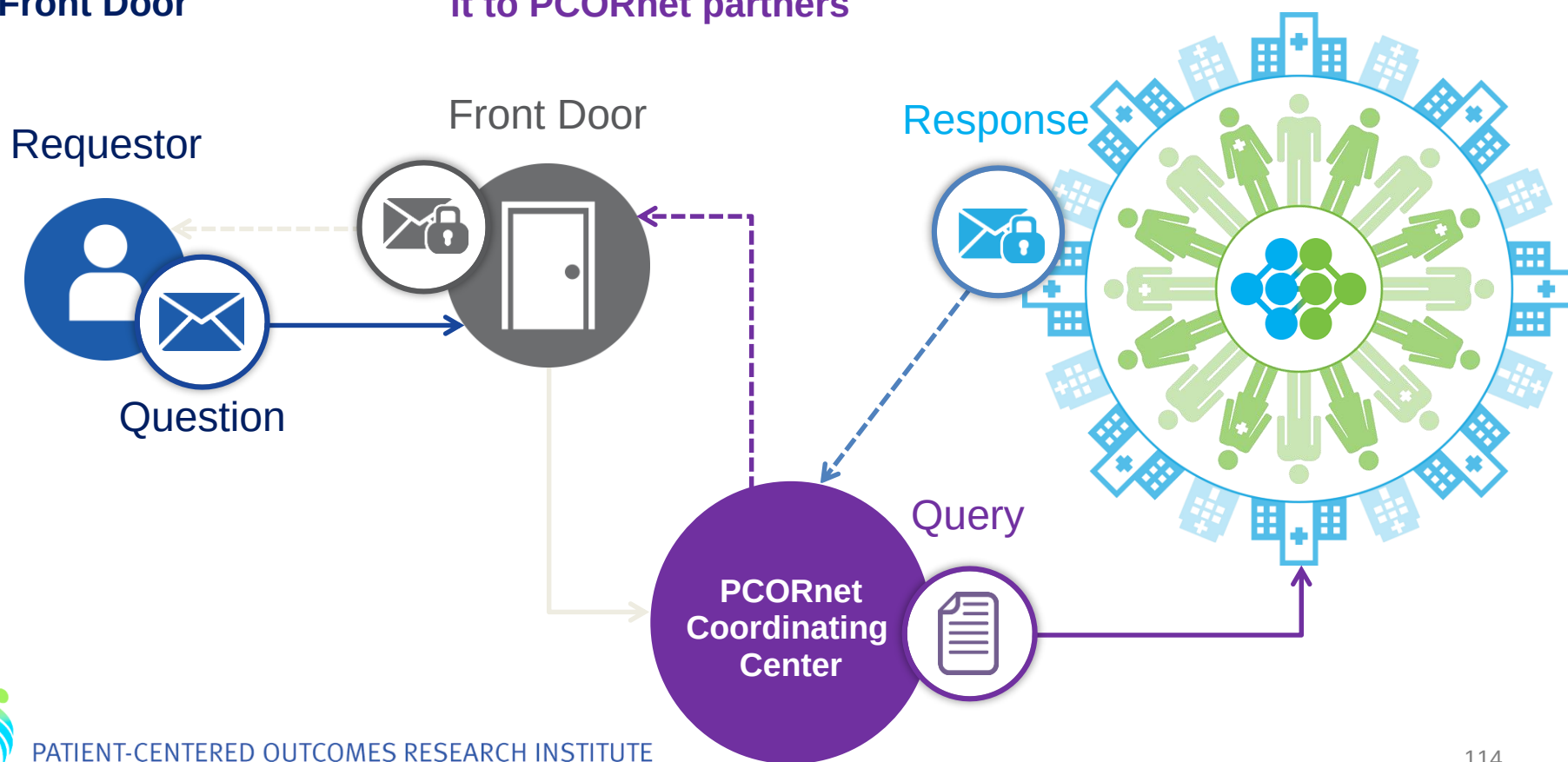


Here's how the PCORnet distributed research network works

The Requestor sends a question to the PCORnet Coordinating Center through the Front Door

The Coordinating Center converts the question into a query with an underlying executable code, and sends it to PCORnet partners

PCORnet partners review the query and provide a response, which is sent back through the Front Door to the Requestor



Developing re-usable, parameterized query tools

Patients AGE RANGE with PROCEDURE and no DIAGNOSIS in the DAYS prior, stratified by AGE, SEX, RACE



Patients 18-65 years old with bariatric surgery and no GI cancer in the 365 days prior to bariatric surgery, stratified by age, sex, race



PCORnet Query Tools

- Menu-Driven Query (MDQ)
 - Simple, point & click cohort definition (e.g., Multiple Sclerosis diagnoses in 2017)
 - Cohort defined by diagnosis and procedure codes, query period, height, weight, age range, etc.
 - Output can be stratified by age group, sex, race, ethnicity, and calendar period
- PCORnet Modular Programs (PMP)
 - More complex cohort logic (e.g., Statin prescription in 2017 with no CVD or Stroke in the year prior) and more comprehensive results
 - Require more time to configure & deploy
- Cohort Quality Assessment (CQA)
 - In-depth quality assessment for specific elements within a cohort



Example of a complex, urgent MDQ- Heart Failure with Preserved Ejection Fraction



Question →
Report
in 8 Business
Days

By Medications (N, % of patients)

ACE inhibitor prescription within the day before or after HFpEF	46,674	13%
ARB prescription within the day before or after HFpEF	31,146	9%
Sacubitril-valsartain prescription within the day before or after HFpEF	29	0%
Spirolactone prescription within the day before or after HFpEF	15,043	4%
Beta Blocker prescription within the day before or after HFpEF	111,620	31%
Loop Diuretic prescription within the day before or after HFpEF	112,108	31%
Thiazide Diuretic prescription within the day before or after HFpEF	12,735	4%
Digoxin prescription within the day before or after HFpEF	11,473	3%
Insulin prescription within the day before or after HFpEF	16,790	5%
SGLT2 Inhibitor prescription within the day before or after HFpEF	13	0%

By Medications (N, % of patients)

ACE inhibitor prescription within the day before or after HFpEF	46,674	13%
ARB prescription within the day before or after HFpEF	31,146	9%
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Insulin prescription within the day before or after HFpEF	16,790	5%
SGLT2 Inhibitor prescription within the day before or after HFpEF	13	0%

By Hospitalizations (N, % of patients)

Inpatient (IP) encounter in the 180 days prior to HFpEF	98,881	28%
Emergency Department (ED) encounter in the 180 days prior to HFpEF	40,756	11%
Emergency Department to Inpatient Hospital Stay (EI) encounter in the 180 days prior to HFpEF	41,360	12%
Observation Stay (OS) encounter in the 180 days prior to HFpEF	9,913	3%
Inpatient (IP) encounter in the 365 days prior to HFpEF	111,825	31%
Emergency Department (ED) encounter in the 365 days prior to HFpEF	48,089	13%
Emergency Department to Inpatient Hospital Stay (EI) encounter in the 365 days prior to HFpEF	46,486	13%
Observation Stay (OS) encounter in the 365 days prior to HFpEF	11,928	3%
Inpatient (IP) encounter in the 1825 days prior to HFpEF	139,653	39%
Emergency Department (ED) encounter in the 1825 days prior to HFpEF	61,782	17%
Emergency Department to Inpatient Hospital Stay (EI) encounter in the 1825 days prior to HFpEF	55,806	16%
Observation Stay (OS) encounter in the 1825 days prior to HFpEF	15,804	4%
Inpatient (IP) encounter in the 365 days after HFpEF	115,202	32%
Emergency Department (ED) encounter in the 365 days after HFpEF	51,955	14%

Querying in PCORnet

- Current capabilities driven by a series of governance decisions
 - Queries will be distributed by the Coordinating Center
 - Network partners can decide whether to run queries and return results
 - Partners have a standard window to return results (10 business days)
- Potential options for the future
 - Development of an X% sample dataset
 - Enable querying of data curation results
 - More rapid turnaround of simple queries



Option 1 – Development of an X% sample dataset

- Partners create a de-identified/anonymized subset of the CDM for X% of their population and submit to a centralized repository. Deploy a query tool so users can interact with the data
- Pros:
 - Real-time response
 - Could allow “public” access
- Cons:
 - Partners will have concerns about misuse of data, risk of re-identification, loss of confidentiality, etc. – may require some risk mitigation from PCRF
 - Costs to develop and validate methods for sampling and de-identification/anonymization - partners may also require their own validation
 - Development and hosting costs of the new query tool and centralized database
- Note: New Common Rule may make this more tractable in the future, depending on how the regulations are interpreted



Option 2 – Enable querying of data curation results

- The Coordinating Center has access to hundreds of univariate statistics that describe the content of the CDM. By sharing these data more broadly, they can be used to answer simple questions and provide a basic overview of the aggregate PCORnet population
- Pros:
 - Relatively low cost / low implementation burden
 - Data exist as aggregate statistics – mitigates partner concerns about re-identification
 - “Real-time” access
- Cons:
 - Current data curation results only support queries for a single criteria/variable (e.g., # of females or # of patients with diabetes, not # of females with diabetes) – could create additional “canned” reports on specific topics/populations to provide greater insight



Option 3 – More rapid turnaround of simple queries

- Take steps to increase network throughput
 - Allow additional authorized users to generate and submit MDQs
 - Modify the MDQ process so that simple queries auto-execute and results are returned **without review**
- Pros:
 - Reuses existing network infrastructure
 - Query response time in seconds/minutes/hours
 - Similar to established approaches by existing networks (e.g., TriNetX, Accrual to Clinical Trials)
- Cons:
 - Will require changes to existing PCORnet governance policies
 - Additional costs to modify network architecture to better monitor status of network partners to ensure uptime/stability
 - Increased support costs for having to manage/train users



Summary

- Option 1 (X% sample) is closest to a searchable tool in the public domain
 - Development costs are non-trivial
 - Will be serious concerns from partners about (re)use of data
- Option 2 (querying data curation), while limited, provides some insight into data behind PCORnet
- Option 3 (more rapid turnaround of queries) tracks activity in networks like ACT; including funders/industry among authorized users who can run queries is similar to the TriNetX model
- All options will increase the overall infrastructure costs for PCORnet – Option 2 is likely the lowest
 - Important to determine external demand & understand how options would affect the marketability of PCORnet
 - Choices not mutually exclusive – could implement Option 2 and decide among others at a later date



PCORnet Dashboard Metrics

Joe Selby, MD, MPH

Executive Director, PCORI



PCORnet Activity Dashboard

- In the March meeting, the PCORI Board suggested that regular dashboard reports are needed for the Network
- Previous and current Network reports have been aimed at internal quality improvement
 - Internal reports designed to highlight status of and progress towards achieving critical infrastructure targets, such as:
 - Track sites as sign on to master DSA and Single IRB (SMART) agreement
 - Monitor query fulfillment and turnaround time
 - Report on data quality



Future Dashboard

- Future dashboards will be designed to inform the Board, the Network, and the public about key PCORnet accomplishments
- For the Board, the dashboards will also serve purpose of providing a longitudinal record of progress on measures important to the health of the Network
- Dashboards will provide both static updates, as well as graphs to depict change over time



Future Dashboard Metrics

- Patient Metrics
 - Number of patients in the Network
 - Number of patients available with an encounter in past 12 months (and therefore likely available for a trial)
 - Number of patients available for Observational study
- Front Door Activity
 - Number of Front Door requests to find network collaborators, overall and by requestor type (e.g., funder, external researcher, network researcher)
 - Number of responses to those requests
 - Number of funded research projects
 - Number and award amount for demonstration and competitive projects funded by PCORI
 - Number and award amount for federally funded projects
 - Number and award amount for industry funded projects



Future Dashboard Metrics

- Research Metrics (for clinical trials, prospective cohort studies)
 - Average days to site activation
 - Average days to first patient enrolled
 - Average enrollment rate
 - Total enrollment
 - Percent of target enrollment achieved
 - Number of trials with data reported
- Number of manuscripts, overall and within studies
- Query Metrics
 - Number of queries executed to date
 - Average query turnaround time
 - Listing of queries (or therapeutic area)
- Administrative Simplicity Metrics
 - Percent signed on to Data Sharing Agreement
 - Percent signed on to single (SMART) IRB agreement



Partnerships to Conduct Research within PCORnet

Cycle 2 2017 Award Slate

Christine Goertz, DC, PhD

Chair, Selection Committee

Joe Selby, MD, MPH

Executive Director



Cycle 2 2017 – Partnerships to Conduct Research within PCORnet

Objective of the PFA

This funding opportunity was directed solely to PPRNs (as prime responders). It is a major step in PCORI's strategy to achieve the Board's vision of a sustainable National research infrastructure. The announcement required applicants to:

- **Develop External Partnerships:** Applicants must collaborate with external stakeholders—industry sponsors or other funding organizations—to secure direct or in-kind support
- **Advance Data Integration:** Applicant PPRNs must describe proposed data linkage(s), how linkages will serve study needs and be accomplished (e.g., using de-identified or identifiable data linkages); and approaches to Institutional Review Board (IRB) oversight of those linkages
- **Generate CER Evidence:** Studies must generate CER evidence relevant to specific conditions, treatments, and patient communities or to clinical care for broader populations
- **Leverage Existing PCORnet Resources:** Applicants must utilize existing PCORnet resources including but not limited to other PPRNs, CDRNs, Health Plans (HPRNs), the Coordinating Center (PCORnet CC), the PCORnet Common Data Model (CDM), and others

PFA DEVELOPMENT APPROVED BY BOARD: June 17, 2017

Funds Available Up To: \$21M total costs



Cycle 2 2017 – Partnerships to Conduct Research within PCORnet

Merit Review Criteria

1. Potential for the study to fill critical gaps in evidence
2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
3. Scientific merit (research design, **data linkage components, leveraging existing PCORnet resources**, and outcomes)
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder engagement (**external partnerships**)



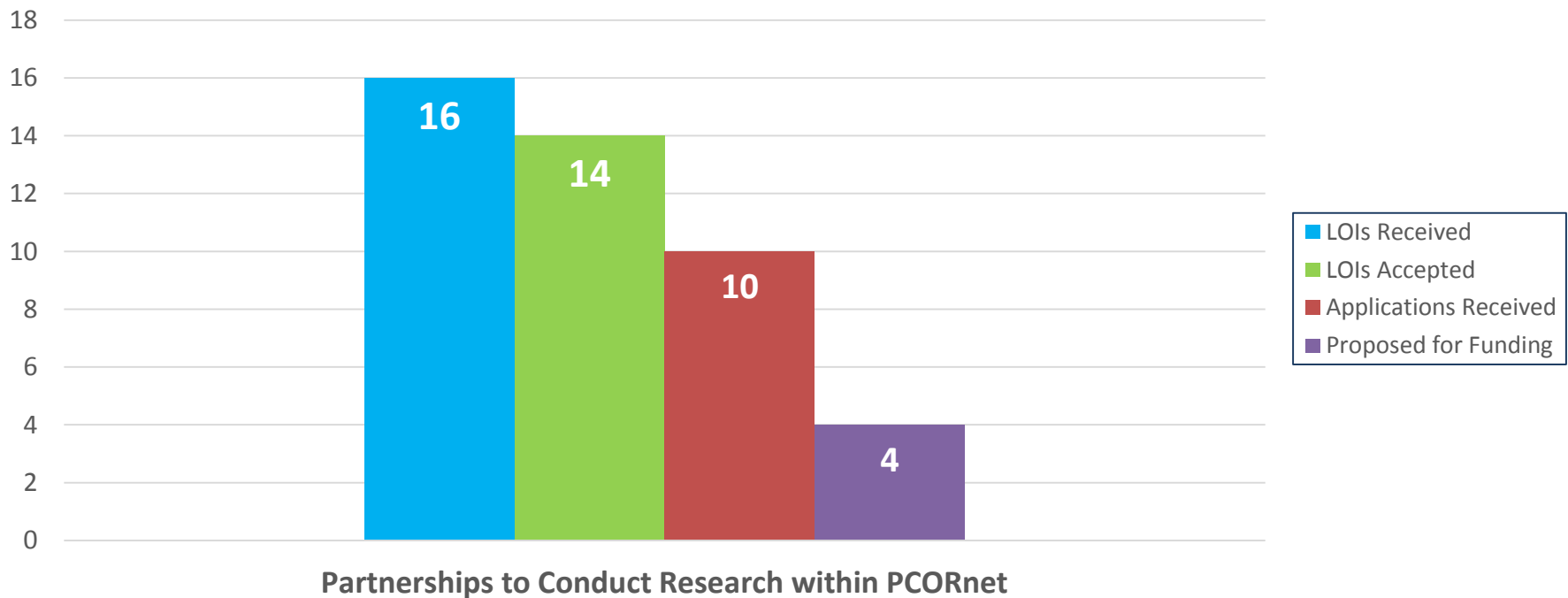
Cycle 2 2017 – Partnerships to Conduct Research within PCORnet

Process Overview

- 16 Letters of Intent (LOIs) submitted
- 14 LOIs invited to submit a full application (**88%**)
- 10 applications were received (**71% of invited LOIs**)

Funding rate is 40 percent

- We are proposing to fund 4 applications* out of 10 received applications



Cycle 2 2017 – Partnerships to Conduct Research within PCORnet

4 Recommended Projects†*

Project
Comparative Effectiveness of Pharmacogenomics for Treatment of Depression (CEPIO-D) (\$4.8M)
Improving Outcomes in Limited Juvenile Idiopathic Arthritis (\$7M)
Using PCORnet to Compare Blood Pressure Control Strategies (\$6.5M)
Comparative Effectiveness of Biologic or Small Molecule Therapies in Inflammatory Bowel Disease (\$2.4M)

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract

† All costs reflect PCORI contributions



Project 1: Comparative Effectiveness of Pharmacogenomics for Treatment of Depression (CEPIO-D)

- **Research Question:** What is the comparative effectiveness of combinatorial pharmacogenomic (PGx) guided treatment to best-practice guideline concordant treatment to improve well-being in adults with major depressive disorder?
- **Population:** Adults ages 18-65 with DSM-IV major depressive disorder, referred by network of 80 clinicians (psychiatrists) from 4 PCORnet CDRNs
- **Intervention:** PGx-guided use of anti-depressants prescribed by clinicians
- **Comparator(s):** Prescription of anti-depressants according to best practice guidelines
- **Outcomes of Interest:**
 - *Primary: WHO-5 patient reported wellness*
 - *Secondary: PHQ-9 depression severity; PROMIS 29 measures ("Ability to Participate in Social Roles and Activities" Index); and a novel m-health depression outcome collected by a smart phone app*
- **Study Design:** Prospective randomized controlled trial
 - Sample Size: 400 (200 per arm)
- **Duration of Active Intervention:** One year
- **Length of Follow-up:** One year
- **Total Project Cost:** \$4.8M



Project 1: Comparative Effectiveness of Pharmacogenomics for Treatment of Depression (CEPIO-D)

- **External Partnership(s):**
 - 2 external partners with contributions totaling ~ \$2M (financial + in-kind)
 - pharmacogenomics lab
 - Personnel, clinician outreach, PGx tests, analysis and training in interpretation
 - m-health manufacturer
 - behavioral analytics platform server license, mobile app license, and implementation services.
- **Advance Data Integration:** PROs, Common Data Model (EMR) from 4 CDRNs, pharmacogenetic, and mobile health data
- **Leverage PCORnet Resources:** PPRN, CDRNs, PCORnet CC and PCORnet Common Data Model



Project 1: Comparative Effectiveness of Pharmacogenomics for Treatment of Depression (CEPIO-D)

- **Potential Impact:**
 - Compares an available and covered diagnostic test to best practice guidelines that has not been conducted in a real world setting
 - Has potential to limit current trial and error nature of treatment decisions and reduce adverse events
- **Patient-Centeredness:**
 - Directly addresses question of how to get to more personalized and effective treatment for depression, sooner
 - Measures PROs selected specifically by patients and clinicians
- **Engagement & Dissemination:**
 - PPRN patient and stakeholder partners, including CDRN leaders “champion” clinician-leaders within the clinical sites at the CDRNs
 - **All Committees will include all collaborators:** quality control, protocol, patient centered priorities, patient stakeholder/ombudsman, and dissemination committees
 - Dissemination committee plan includes dissemination via social media, radio and TV, print as well as eNewsletters



Project 2: Improving Outcomes in Limited Juvenile Idiopathic Arthritis

- **Research Question(s):**
 - Does early initiation of a biologic agent (abatacept) prevent disease extension in limited Juvenile Idiopathic Arthritis (JIA) compared to standard treatment with NSAIDS and articular injections?
- **Population:**
 - Children 2-16 y/o within 6 months of clinical diagnosis of JIA, arthritis affecting 1-4 joints, clinically active arthritis of at least 1 joint at the time of enrollment, and willing to enroll in the registry (and parents) identified from 61 sites affiliated with the registry and from 4 sites affiliated with one CDRN
- **Intervention and Comparator:**
 - Abatacept + Usual care (NSAIDS and glucocorticoid joint injections) v. usual care alone
- **Outcomes of Interest:**
 - *Primary: progression to “polyarthritis” (≥ 5 joints affected) or presence of inflammation of the uvea (the pigmented layer of the eye);*
 - *Secondary: PRO measures related to global health, functional ability, pain, fatigue, depression, anxiety, medication side effects, family impact*



Project 2: Improving Outcomes in Limited Juvenile Idiopathic Arthritis

- **Study Design:** Randomized Controlled Trial
 - Sample Size:
 - 306 patients (153 per arm)
- **Duration of Active Intervention:** 24 weeks
- **Length of Follow-up:** 18 months
- **Total Project Cost:** \$7M



Project 2: Improving Outcomes in Limited Juvenile Idiopathic Arthritis

- **External Partnership(s):**
 - 3 external partners with contributions totaling ~ 1.7M (in-kind)
 - Pharmaceutical company
 - Study drug and support of ethnographic work
 - Patient foundation
 - personnel, data sharing, patient and caregiver dashboards, treatment algorithms
 - Disease registry
 - Research Data Warehouse management & QA, software modifications & operational support
- **Data Integration:** Registry (clinical and PRO), EMR, survey data
- **PCORnet Resources:** CDRN, PCORnet CC, Common Data Model



Project 2: Improving Outcomes in Limited Juvenile Idiopathic Arthritis

- **Potential Impact:**
 - The significance of the scientific question goes beyond rheumatology. If the study suggests early aggressive treatment can change the life-long course of this autoimmune inflammatory disease, it may have relevance to treatment of numerous other inflammatory disease treatments, e.g., Inflammatory Bowel Disease
 - The proposed HTE analysis based on disease severity at diagnosis is of great interest given the range of conditions (disease heterogeneity) that fall under the umbrella of Juvenile Idiopathic Arthritis (JIA)
- **Patient-Centeredness:**
 - Patients and parents expressed profound interest in this question: can earlier treatment prevent progression, adverse consequences and impaired QOL
 - Research has potential to give parents and children answers, allowing them to avoid complications, and have a better quality of life
- **Engagement & Dissemination:**
 - An Engagement Core will be trained through a Patient Centered Research 101 workshop (developed by the PPRN). This group will oversee patient centeredness for all aspects of study research and human subjects protection
 - Detailed dissemination plan to include multiple audiences and modalities for outreach



Project 3: Using PCORnet to Compare Blood Pressure Control Strategies

- **Research Question(s):**
 - **Clinic RCT:** Compares two levels of support provided to clinics and institutions for improving population blood pressure control rates
 - **Device RCT:** Compares home blood pressure monitoring with standard home blood pressure cuff to monitoring with a Bluetooth® enabled cuff with enhanced reporting of blood pressure levels to patient and to physician
- **Population:**
 - **Clinic RCT:** Clinics from within 2 PCORnet CDRNS whose member sites are willing to participate in the blood pressure program, adults 18-85, ≥ 1 outpatient encounter with hypertension diagnosis
 - **Device RCT:** Adults ≥ 20 , SBP > 145 , at least one ambulatory visit, own a smart phone
- **Intervention and Comparator(s):**
 - **Clinic RCT:** Full Support: practice facilitator for participating clinics vs. Self-serve Support: in the form of the materials and orientation webinar of blood pressure program
 - **Device RCT:** Bluetooth® enabled blood pressure cuff for home blood pressure monitoring vs. Standard cuff for home blood pressure monitoring



Project 3: Using PCORnet to Compare Blood Pressure Control Strategies

- **Outcomes of Interest:**
 - Primary: **Clinic Trial:** *Blood pressure control among patients with hypertension*
Device Trial: *Demonstrated attainment of individual blood pressure goal*
 - Secondary: *(both trials)*
 - *Blood pressure reduction, Measurement quality index (proportion of clinic visits with at least 1 uncontrolled blood pressure with 2 or more measurements during last visit), Therapeutic inertia index (proportion of clinic visits with uncontrolled blood pressure that are not associated with a prescription for a new or increased dose of blood pressure medication), Adherence index among patients with uncontrolled hypertension, Demonstrated attainment of individual blood pressure goal (by clinic or home)*
- **Study Design:** Clinic Trial: Cluster RCT
Device Trial: Individual-level RCT
- **Sample Size:** Clinic RCT= 20 clinics
Device RCT= 2,000 patients
- **Duration of Active Intervention:** Clinic Trial: 18 months; Device RCT: 12 month
- **Follow-up:** Clinic Trial: 6/12/18 months; Device Trial: 1/3/6/12 months
- **Total Project Cost:** \$6.5M



Project 3: Using PCORnet to Compare Blood Pressure Control Strategies

- **External Partnership(s):**
 - 2 external partners with contributions totaling ~1.5M (financial + in-kind)
 - Very large disease advocacy organization
 - Personnel, overall study support and travel
 - Very large physician advocacy organization
 - Personnel, overall study support and travel
- **Data Integration:** Common Data Model (EMR), Registration and follow-up data, PROs, and Device data
- **PCORnet Resources:** PPRN (Research Platform), PCORnet CC, Common Data Model, CDRNs (recruitment, SMART IRB, Health System engagement), Cardiovascular disease collaborative research group (CRG) for refining the topic and developing the proposal



Project 3: Using PCORnet to Compare Blood Pressure Control Strategies

- **Potential Impact:**
 - Poor blood pressure control remains a prevalent issue – even small improvement in blood pressure control at the clinic level could have a nation-wide impact on mortality
- **Patient-Centeredness:**
 - Clinic Trial: helps patients indirectly by supporting effective program implementation
 - Device Trial: directly helpful to patients for choosing more effective home monitoring technology
- **Engagement & Dissemination:**
 - The PPRN held a formal Patient-Centered Review
 - Engaged multiple patient groups, intense engagement with 12 patients and the study team, as well as a follow up survey completed by 177 patients
 - Study partners run the program that will immediately be able to use and disseminate the results of the study



Project 4: Comparative Effectiveness of Biologic or Small Molecule Therapies in Inflammatory Bowel Disease

- **Research Questions:**
 - **Crohn's Disease:** What is the comparative effectiveness of second-line biologic agents (vedolizumab vs. ustekinumab) among patients who are anti-TNF primary or secondary non-responders?
 - **Ulcerative Colitis:** What is the effectiveness of a second line biologic agent (vedolizumab) vs. small molecule (tofacitinib) among patients who are anti-TNF primary or secondary non-responders?
- **Population:** Adult Crohn's Disease and adult Ulcerative Colitis patients, non-responsive or lost response to anti-TNF biologics
- **Intervention and Comparator:**
 - **Crohn's Disease:** Ustekinumab v. Vedolizumab
 - **Ulcerative Colitis:** Tofacitinib v. Vedolizumab

} (both studies use new-user design cohorts)



Project 4: Comparative Effectiveness of Biologic or Small Molecule Therapies in Inflammatory Bowel Disease

- **Study Design:** For both Crohn's Disease and Ulcerative Colitis:
 - **Prospective Cohort (for evaluating PROs)**
 - Patients recruited from two HPRNs and from a multi-center cohort of adult IBD patients with longitudinal collection of clinical and patient-reported data and biosamples, with the PPRN portal/survey system uses for collecting data
 - **Retrospective Cohort (for evaluating treatment continuation, hospitalizations, surgery)**
 - Based completely in PCORnet's 2 HPRNs and using CDM
 - **Sample Size:** Prospective: 382 patients with each condition
Retrospective: ~994 patients with each condition
- **Outcomes of Interest:**
 - **Prospective:** Primary: PRO measures of Pain Interference and Fatigue 6 months after treatment initiation, continuation of treatment for >1 year; Secondary: additional PROMIS domains (sleep disturbance, social satisfaction, anxiety and depression) or disease specific symptom index (CD/UC activity index)
 - **Retrospective:** Primary: Persistence of treatment at 1 year; Secondary: all cause hospitalization and need for abdominal surgery
- **Timeline:** Follow-up at 26 weeks following treatment initiation (Prospective studies); 52 weeks following treatment initiation (Retrospective studies)
- **Total Project Cost:** \$2.4M



Project 4: Comparative Effectiveness of Biologic or Small Molecule Therapies in Inflammatory Bowel Disease

- **External Partnership(s):**
 - 1 external partner with contributions totaling ~\$820,000 (financial + in-kind)
 - large patient advocacy-research foundation
 - Patient engagement and support of Inflammatory bowel disease cohort
- **Advance Data Integration:** Clinical, Claims and PROs
- **Leverage PCORnet Resources:** 2 PPRNs, 2 HPRNs, and the PCORnet CC



Project 4: Comparative Effectiveness of Biologic or Small Molecule Therapies in Inflammatory Bowel Disease

- **Potential Impact:**
 - Inflammatory Bowel Disease (IBD) is a very expensive and chronic, morbid disease. Many patients do not respond to the first line treatment or ultimately stop responding to treatment. The proposed study fills a critical knowledge gap in determining which treatment is most effective after primary treatment fails
- **Patient-Centeredness:**
 - This research was highly prioritized by patients involved in the PPRN
 - The design of the study focuses on outcomes that matter to patients with Inflammatory bowel disease
- **Engagement & Dissemination:**
 - This study includes a study specific patient engagement plan that leverages the lessons learned from the PPRN and broader PCORnet experience
 - This includes two patient co-investigators who will be a part of the study at all stages including recruitment, retention and dissemination of findings to patients



Cycle 2 2017 – Partnerships to Conduct Research within PCORnet

*4 Recommended Projects**

PFA	Amount Budgeted	Proposed Total Award
Partnerships to Conduct Research within PCORnet	\$21 Million	\$20.8 Million

* All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract



Board Vote

Call for a Motion to:

- **Approve** funding for the recommended slate of awards from the Cycle 2 2017 Partnerships to Conduct Research within PCORnet PFA

Call for the Motion to Be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative Motion**

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions



Public Comment Period

Kristin Carman, MA, PhD

Director, Public and Patient Engagement



Wrap Up and Adjournment

Grayson Norquist, MD, MSPH
Chairperson, Board of Governors

