Advisory Panel on Rare Disease Spring 2015 Meeting

Washington, DC

May 27, 2015

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Welcome and Plans for the Day

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI
Marshall L. Summar, MD
Chair, Advisory Panel on Rare Disease, PCORI
Vincent Del Gaizo
Co-Chair, Advisory Panel on Rare Disease, PCORI

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Housekeeping

- Today's webinar is open to the public and is being recorded.
- Members of the public are invited to listen to this teleconference and view the webinar.
- Anyone may submit a comment through the webinar chat function or by emailing advisorypanels@pcori.org.
- Visit www.pcori.org/events for more information.
- Chair Statement on COI and Confidentiality

Today's Agenda

Start Time	Item	Speaker
8:30 a.m.	Welcome and Plans for the Day	B. Luce M. Summar V. Del Gaizo
8:45 a.m.	Rare Disease Research Standards Landscape Review	N. Whitehead
10:15 a.m.	Break	
10:30 a.m.	PCORI's **DRAFT** Guidance on PCOR for Rare Diseases	A. Anise D. Whicher
11:30 a.m.	Pipeline to Proposal Awards	C. Clyatt
12:00 p.m.	Lunch	
1:00 p.m.	CTAP Subcommittee on Recruitment, Accrual, and Retention	M. Michaels
2:00 p.m.	Follow-up Analysis of Letters of Intent (LOIs) on Rare Diseases: Spring 2015 Cycle	L. Forsythe V. Gershteyn L. Fayish

Today's Agenda (cont'd.)

Start Time	Item	Speaker
2:30 p.m.	Exploring the Eugene Washington PCORI Engagement Award Program	L. Hotchkiss
3:00 p.m.	Break	
3:15 p.m.	Potential Uses for Chatter	E. Djabali
3:30 p.m.	Recap and Next Steps	B. Luce M. Summar V. Del Gaizo
3:45 p.m.	Adjourn	

PCORI Scientific Leads to the Advisory Panel on Rare Disease

- **Ayodola Anise, MHS – Program Officer in the Addressing Disparities Program**

Before PCORI, Anise worked for the Engelberg Center for Health Care Reform at the Brookings Institution, where she managed activities related to the Quality and Equity/Disparities Initiatives. Her work there focused on informing regional, state, and national practices on performance measurement, specifically addressing data collection, data integration/aggregation, patient-centered measurement, and vulnerable populations.

Prior to joining Brookings, Anise worked as a senior associate for The Lewin Group, a health care research and consulting firm, and as project coordinator at Georgetown University on a Centers for Disease Control and Prevention-funded longitudinal study of women experiencing intimate partner violence. Anise has experience working with low-income and minority populations, conducting qualitative and quantitative data collection and analysis, and performing evidenced-based literature reviews.

- **Danielle Whicher, PhD, MHS – Program Officer for the Clinical Effectiveness Research (CER) program**

Before joining PCORI, Whicher was a project coordinator at the Johns Hopkins Berman Institute for Bioethics. In this role, she worked on research designed to engage patients and other stakeholders in conversations about appropriate approaches to disclosure and authorization for enrolling patients in CER studies. Whicher previously was a project manager at the Center for Medical Technology Policy. At CMTP, she managed a number projects designed to engage stakeholders in discussions about the design of CER studies, as well as in activities that aimed to develop prioritized research agendas for different high-priority research topics.

She has authored a number of manuscripts on policy, methods, and CER-related ethics issues, and was a guest lecturer for the Introduction to Comparative Effectiveness and Outcomes Research course at the Johns Hopkins Bloomberg School of Public Health.

Rare Disease Research Standards Landscape Review

Nedra Whitehead, PhD

Task Leader, RTI International, Division of Statistics and Epidemiology

Purpose

Compile and identify gaps in standards for rare disease research.

Rare disease registry best practices

- Design
- Management

Biospecimen best practices

- Stewardship
- Biobanks

Research

- Study designs
- Strength of evidence

Methods

Landscape, not systematic, review

- Reflect current practices and opinions
- Highly relevant and recent publications

Publications

PubMed search
- Predetermined and ad hoc search terms

Referred by
- Rare Disease Advisory Working Group
- RTI Project Team

Websites

Referenced in publications

Identified by Internet searches

Referred by RTI project team member

We reviewed promising references, regardless of where cited.

Definitions of Rare Disease

- Often set by legislation
- Vary by country or jurisdiction
- Include prevalence as proportion or number of affected individuals
  - Range from 1 to 6.3 per 10,000
- May include factors such as severity or lack of treatment

We included relevant publications regardless of their definition of rare disease.

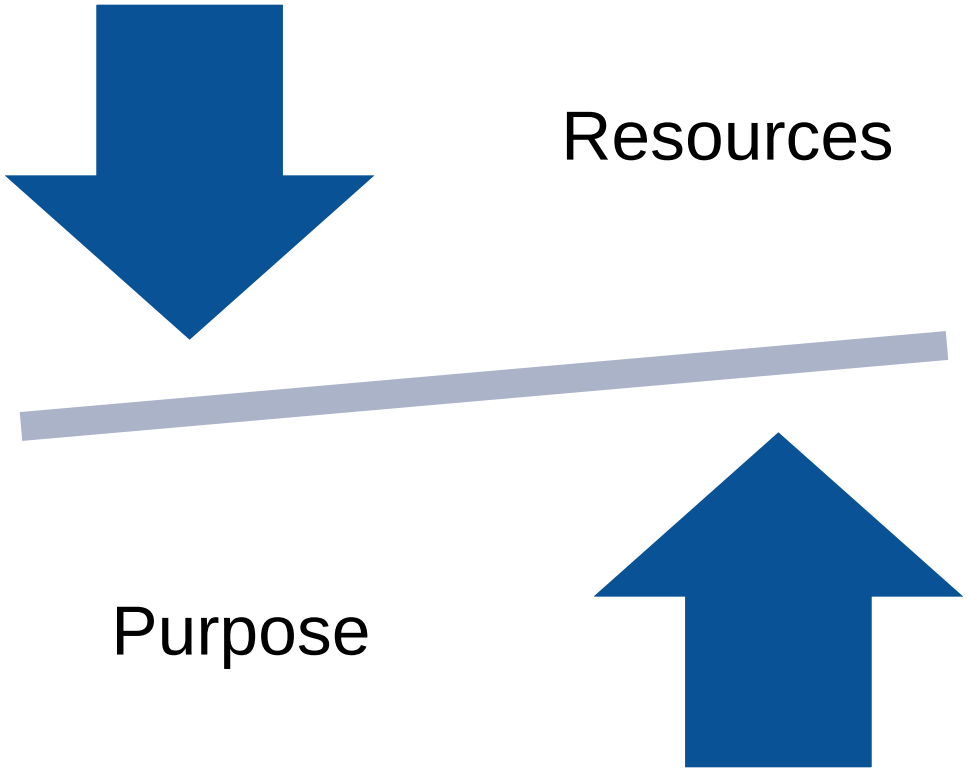
Rare Disease Registries Best Practices

Definitions of Registries

Patient Registry	Organized system that collects uniform data
	Population defined by particular disease, condition, or exposure
	Predetermined scientific, clinical, or policy purposes[1]
Research Registries	Above ✚
	Storage, retrieval, and dissemination of data
	Collection of identifiable information[2]

[1] Gliklich, R., N. A. Dreyer, M. B. Leavy, P. Velentgas, and L. Khurana. 2012. Standards in the Conduct of Registry Studies for Patient-Centered Outcomes Research. edited by P.-C. O. R. Institute. Washington, DC.
[2] Richesson, R., and K. Vehik. 2010. Patient registries: utility, validity and inference. In *Advances in Experimental Medicine and Biology*, 87-104.

Design Considerations



Questions to Consider

What is the **purpose** of the registry?

How might the characteristics of the disease **affect the design or quality** of a registry?

Is there an **existing registry** that fulfills the purpose?

What **resources are needed** to design the registry?

What is the **population** of interest?

Is **funding available** to implement and maintain the registry?

Purposes of Rare Disease Registries

Focal point for information on individuals with a rare disease

Data collection for surveillance, research, or evaluation of interventions

Research Recruitment

- Clinical trials of drugs or other interventions
- Surveys or other studies focused on specific issues

Possible Uses of Registry Data

Monitoring

- Natural history
- Patient experiences
  - Diagnosis
  - Barriers to treatment
- Postmarket outcomes and adverse events
  - Less common adverse effects
  - Effectiveness of treatment in clinical practice

Improving clinical practice

- Effectiveness of therapies
- Attributes of patients for whom a therapy is most effective
- Identify clinics with better or worse patient outcomes

Recruitment for additional research

- Increased efficiency

Is a Registry Needed?

Is there an **existing registry** that draws from the population of interest and fulfills the purpose?

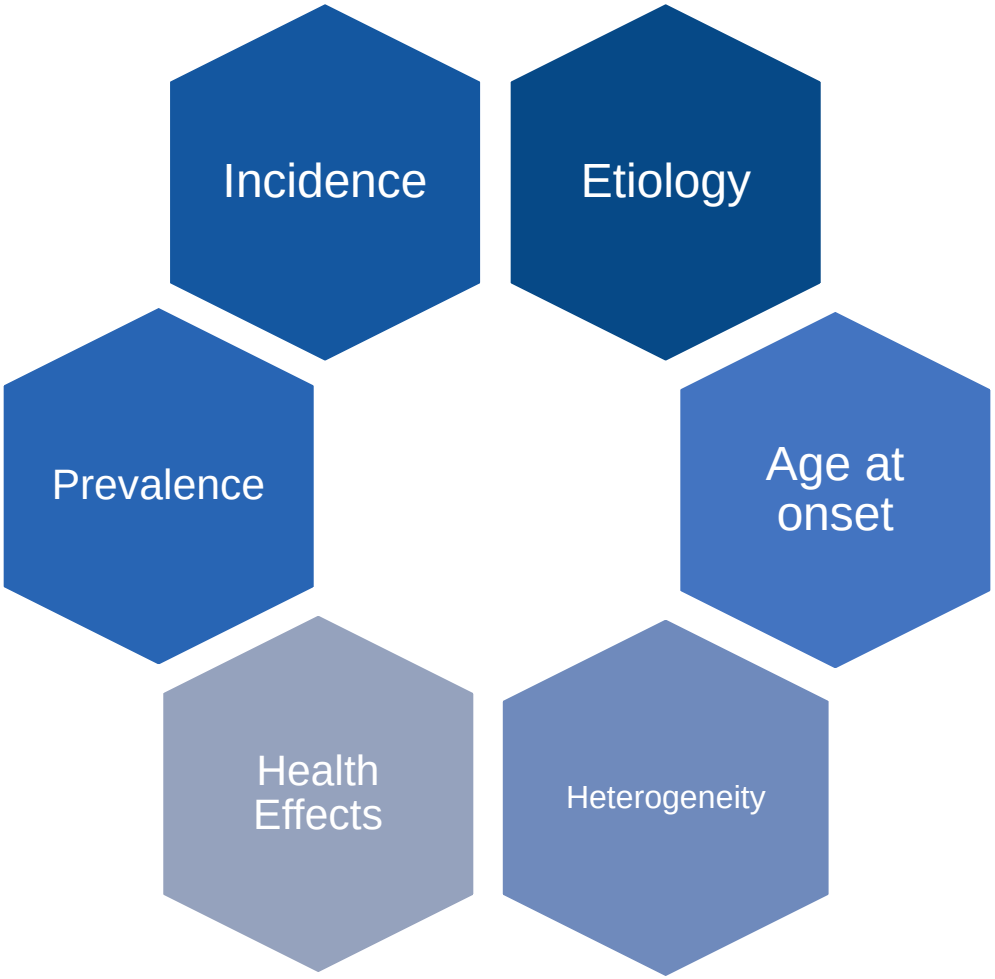
Organization	Comments
Agency for Healthcare Research and Quality	In addition to listing existing patient registries, serves as an archive for expired registries
National Institutes of Health	Lists only national registries
Orphanet	European RD registries
RD-Connect	Global consortium of RDs; includes a directory of member registries

Two registries that have the same purpose and draw from the same population is inefficient and may compromise the representativeness of both registries.

Registry Design

Characteristics of Rare Diseases

The characteristics of the specific rare disease influences registry design.



Case Definition

Based on disease/group of diseases, not therapy or intervention

Narrow versus expansive

- Homogeneity versus full spectrum of disease
- Workload and costs

Inclusion or exclusion criteria

- Age at diagnosis or onset of symptoms
- Diagnostic specificity
- Clinical symptoms or severity
- Geographic area
- Demographic characteristics

Case Ascertainment

Passive

Solicits enrollment by patients or clinicians.

- Online registry for neurofibromatosis type 1 recruited 880 participants, 72% of whom became aware of the registry through Facebook[1]

Validity of patient-reported diagnosis documented in at least two registries[2]

Representativeness of enrollees is a major concern

Active

Searches for all cases within the study population

Specific diagnostic codes

Algorithms

- To identify patients[3]
- Assess the accuracy of coding[4]
- Did not identify reports of ascertainment by electronically scanning of electronic medical records

[1] Johnson, K. J., N. L. Mueller, K.E. Williams, and D. H. Gutmann. 2014. Evaluation of participant recruitment methods to a rare disease online registry. *American Journal of Medical Genetics Part A* 164 (7):1686-1694.
[2] Allen, K. D., E. J. Kasarskis, R. S. Bedlack, M. P. Rozear, J. C. Morgenlander, A. Sabet, L. Sams, J. H. Lindquist, M. L. Harrelson, C. J. Coffman, and E. Z. Oddone. 2008. The National Registry of Veterans with Amyotrophic Lateral Sclerosis. *Neuroepidemiology* 30 (3):180-190.
[3] Nigwekar, S., C. Solid, E. Ankers, R. Malhotra, W. Eggert, A. Turchin, R. Thadhani, and C. Herzog. 2014. Quantifying a rare disease in administrative data: the example of calciphylaxis. *Journal of General Internal Medicine* 29 (3):724-731.
[4] Kaye, W. E., M. Sanchez, and J. Wu. 2014. Feasibility of creating a national ALS registry using administrative data in the United States. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration* 15 (5-6):433-439.

Data Sources

- Medical records
- Administrative data, such as hospital discharge summaries; insurance records, including Medicaid and Medicare; and birth and death certificates
- Patients and families
- Clinicians
- Pharmaceutical records

Data Elements

- Data specific to the registry purpose
- Common data elements for rare disease registries
  - Standard variable definitions, code lists, and instructions
    - GRDR® Program[1]
    - EPIRARE project for the European platform for RD patient registration[2]; and
    - The French national Minimum Data Set for Rare Diseases, which are very similar to the CDEs developed for the GRDR® [3]

Domains	Domains
Current contact information	Diagnosis
Sociodemographic	Family history
Contact and communication preferences	Birth and reproductive history
Administrative	Anthropometric
Clinical research participation and biospecimens	Patient-reported outcomes
Outcomes	Medications, devices, and health services

[1] Rubinstein & McInnes, 2015 [2] Taruscio et al., 2014 [3] Choquet et al., 2015.

Data Quality

Representativeness of registry

Self-selection bias in persons who seek diagnosis or participate

Undiagnosed cases

Lead-time bias

Systematic differences in the age or severity of morbidity at diagnosis

Misclassification bias

Misdiagnosis associated with patient characteristics

Information bias

Bias in completeness or accuracy of data

Ethical Issues

IRB

HIPAA compliance

Will information be returned to participants?

Aggregate data only?

Clinically relevant only?

All individual's test results or clinical findings?

Participant incentives or compensation?

Update and Modifications

Changes in purpose, sponsor, or technical infrastructure

- May require assessment similar to original design

Operational problems or errors

Best practice – Include update process in design.

Management Policies

Governing structure

- Determined by sponsorship, purpose, and stakeholders
- Mechanisms for:
  - Obtaining stakeholder input
  - Evaluating whether the registry is fulfilling its purpose

Administration

- Registrar
  - Primary responsibility for design and implementation of the registry
  - Responsible for stewardship of the registry's data and implementation of data access policies

- Registrar and staff
  - Create, maintain, and implement the registry's protocol
  - Maintain the database
  - Promote its use
  - Arrange for its evaluation

Data Access

- Requests for analysis increase use and impact of the registry data
- As awareness of registry data grows, demand often increases
- Policies
  - Data sharing and data use agreements
  - Public use datasets
- Data access portals can
  - Provide access to registry data without access to raw data
  - Allow simple or complex data queries
  - Examples:
    - Orphanet portal
      - Provides information on rare disease research, orphan drugs, and other topics
    - GRDR® repository
      - Integrates data across rare disease registries for cross-disease analyses and biomedical studies

Inter-registry Compatibility

Infrastructure software for web-based rare disease registries

- National Organization for Rare Disorders
- NCATS
  - Developed by Marshfield Clinic Research Foundation
  - Supports the GRDR®

Common data model

- Allow same analyses to be run against multiple datasets with minimal modification
- Observational Medical Outcomes Partnership CDM[1]

[1] Overhage, Ryan, Reich, Hartzema, & Stang, 2012.

Biospecimens and Biobanks

Biospecimens

Include tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, or other bodily fluids.

Collected by patients, through routine clinical procedures or additional medical procedures

Expensive to collect and maintain

Good stewardship

- Ensures preservation of the specimens from collection through use
- Fosters sharing
- Maximizes value obtained from specimens
- Protects participant privacy

Biobanks

- Developed for current and future biomedical research purposes
- Collect, process, store, and distribute biological materials for medical research
- Maintain quality of biospecimens and associated data profile
- Make specimens available for widest possible range of scientific research

Virtual biobanks

- Electronic integration of specimen and associated data through a common data registry
- Accessible worldwide regardless of where specimens are stored
- Provides ability to review data without access to physical sample
- Multiple locations that implement a common storage environment
- Network of multiple biobanks with same minimum biobanking and data sharing standards

Ethical Considerations

Informed consent

- Identify all intended uses of biospecimens and associated information
- Identify any possible commercial intentions or sponsorship by commercial organizations
- Identify plans for archiving DNA or creating immortalized cell lines
- Present plans for distribution of genetic materials to secondary users

Privacy

- Develop plans and policies to prevent re-identification of subjects

Recontact and returning results

- Develop policies for recontacting subjects for additional information
- Detail policies for return of research test results
- Detail policies for return of incidental findings

Logistical Considerations

Maximization of biological information obtainable

- Collection, transport, and storage procedures
- Conservation of specimens
- Quality control procedures
- Location management
- Duration of storage

Governance

- Data and sample ownership
  - Per US Appeals Court: Donors do not retain an ownership interest
- Data and sample distribution processes
- Resources for support and maintenance

Study Design for Rare Diseases

Rare Disease Study Design and Implementation Issues

Difficulty in recruiting an adequate and representative sample

Infrequent or clustered health outcomes

Heterogeneity
- Genotype
- Genomic background
- Environmental interaction

Privacy and ethical concerns
- Risk of re-identification

Adaptations of Study Designs

Reduce heterogeneity

- Limit by severity, phenotype, or genotype

Reduce need for controls

- Crossover designs - participants are their own controls
- Historical controls

Designs that reduce time on placebo

- Enhance participation
- Reduce ethical concerns

Increased observed outcomes

- Longer follow-up
- Surrogate markers
- Continuous outcome measures

Algorithms for Choosing Study Design

Gupta et al., 2011

- Examines designs that address limited number of available participants

- Questions relate to
  - Predictability and duration of effect
  - Stability of the disease course
  - Participant retention
  - Availability of the required number of participants
  - Time between inclusion and outcome assessment compared with accrual time
  - If planned sample size can be reasonably recruited

Cornu et al., 2013

- Sample size
- Reversibility of outcome
- Rapidity of response
- Minimization of time on placebo
- Active treatment provision at the end of the trial
- Controls within or across patients

Strength of Evidence Assessments

Study limitations

- Adaptations to study designs may be at more risk of bias
- Small sample designs may be at increased risk of random error

Directness

Adaptations for rare disease may result in more indirect evidence

Consistency

Rare disease literature may be less likely to have at least two independent studies

Precision

Rare disease studies are more likely to be small and have greater imprecision

Reporting bias

Limited to studies with a prospectively reported protocol

Other Assessments

Optional domains

- Dose response association
  - Strong relationship between dose and response may increase confidence
- Uncontrolled confounding
  - Small sample sizes may impede control for confounding and decrease confidence
- Magnitude of effect
  - A large effect may increase confidence

Mechanistic evidence

- Formal approach to integrate knowledge of how the intervention works into the evaluation of the intervention

Gaps

- Standards for assessing and improving representativeness of self-enrollment registries
- Methods for decision making with inadequate evidence

More Information

Nedra Whitehead, PhD, MS, CGC
Director, Center for Genomics in Public Health and Medicine

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Ellen Bishop
Research Statistician
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Break

10:15 – 10:30 a.m.

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PCORI's DRAFT Guidance on PCOR for Rare Diseases

Ayodola Anise, MHS
Program Officer, PCORI
Danielle Whicher, PhD, MHS
Program Officer, PCORI

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Purpose: PCORI's Guidance on Research in Rare Diseases

- To provide guidance to applicants planning to propose research studies in rare diseases* for PCORI funding
- To provide guidance to staff responsible for reviewing LOIs and applications

- Developed based on structured meetings of PCORI science staff
  - Discussion topics were informed by questions PCORI staff received from applicants wishing to propose research studies in rare diseases

*According to the Rare Disease Act of 2002, rare diseases are those that affect fewer than 200,000 people in the United States

Discussion Questions

- Are there potential challenges with research in rare diseases that are not addressed in this guidance?
- Is this guidance sufficiently clear? Does it sufficiently address the decisions investigators encounter when thinking about appropriate comparators?
- What is feasible in terms of research in rare diseases if these are the parameters applicants are asked to work within?

What Type of Research Does PCORI Fund?

- PCORI funds patient-centered CER that addresses outstanding evidence gaps in the prevention, diagnosis, and treatment of rare diseases.
  - Comparisons of evidence-based and/or commonly used interventions

Demonstrating that Interventions Are "Commonly Used"

- Applicants must:
  - Make the case that their study addresses a realistic clinical choice faced by patients and their providers
  - Define the comparators and describe how the interventions being studied are currently used in clinical practice (e.g., numbers of prescriptions filled)
- PCORI prefers comparisons of two interventions. If this is not possible, applicants should specify what the control group will receive (e.g., supportive services) and how this will be measured

Demonstrating that Interventions Are "Evidence-Based"

- Applicants must:
  - Describe the existing efficacy/effectiveness data on the proposed interventions, even if the data are limited, and provide citations
  - If unpublished, explain why
- PCORI may consider applications that involve interventions with limited efficacy/effectiveness data *if* the application addresses a realistic and important clinical choice

Consultation

- RDAP Expert Subcommittee: Provide advice to PCORI staff on questions related to rare disease research

- CTAP Expert Subcommittee: Provide guidance to PCORI staff on questions related to specific methodological designs

Discussion Questions

- Are there potential challenges with research in rare diseases that are not addressed in this guidance?
- Is this guidance sufficiently clear? Does it sufficiently address the decisions investigators encounter when thinking about appropriate comparators?
- What is feasible in terms of research in rare diseases if these are the parameters applicants are asked to work within?

Pipeline to Proposal Awards

Courtney Clyatt, MA, MPH
Senior Program Associate, Engagement, PCORI

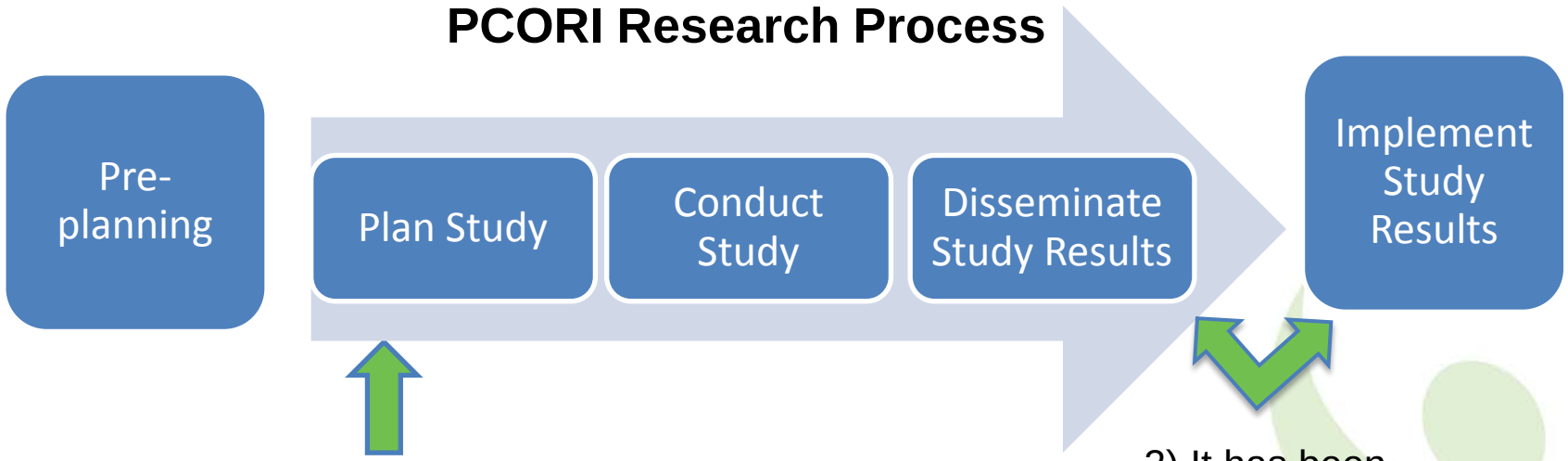
Overview

- P2P Origin and Mission
- Where P2P Falls in the PCORI Research Enterprise
- How P2P Ties to PCORI Engagement Goals
- P2P Structure and Infrastructure
  - Program and Award Management
  - Review and Evaluation
- Funded Rare Disease P2P Projects

Pipeline to Proposal Awards (P2P)

- Mission: P2P aims to build a national community of patient, stakeholder, and researcher partnerships that have the expertise and passion to participate in patient-centered outcomes research within their community that leads to high-quality research.
- Purpose:
  - Build community
  - Form or strengthen reciprocal relationships between researchers and non-research communities
  - Support capacity building, co-learning, and the development of a sustainable infrastructure to facilitate “research done differently”
  - Accelerate proposal submission (or re-submission)
  - Speed Dissemination and Implementation

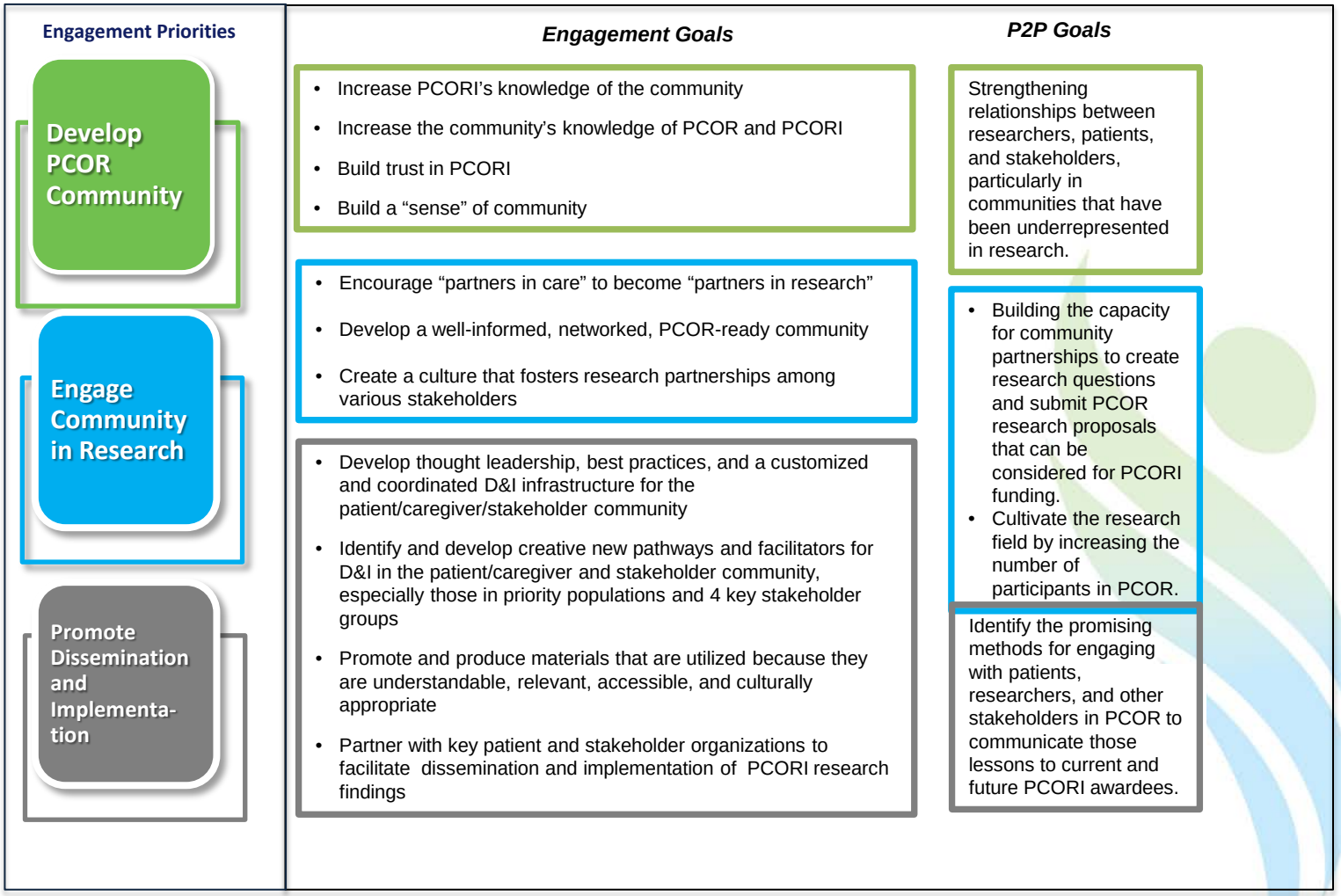
P2P Awards Strengthen the PCORI Research Enterprise



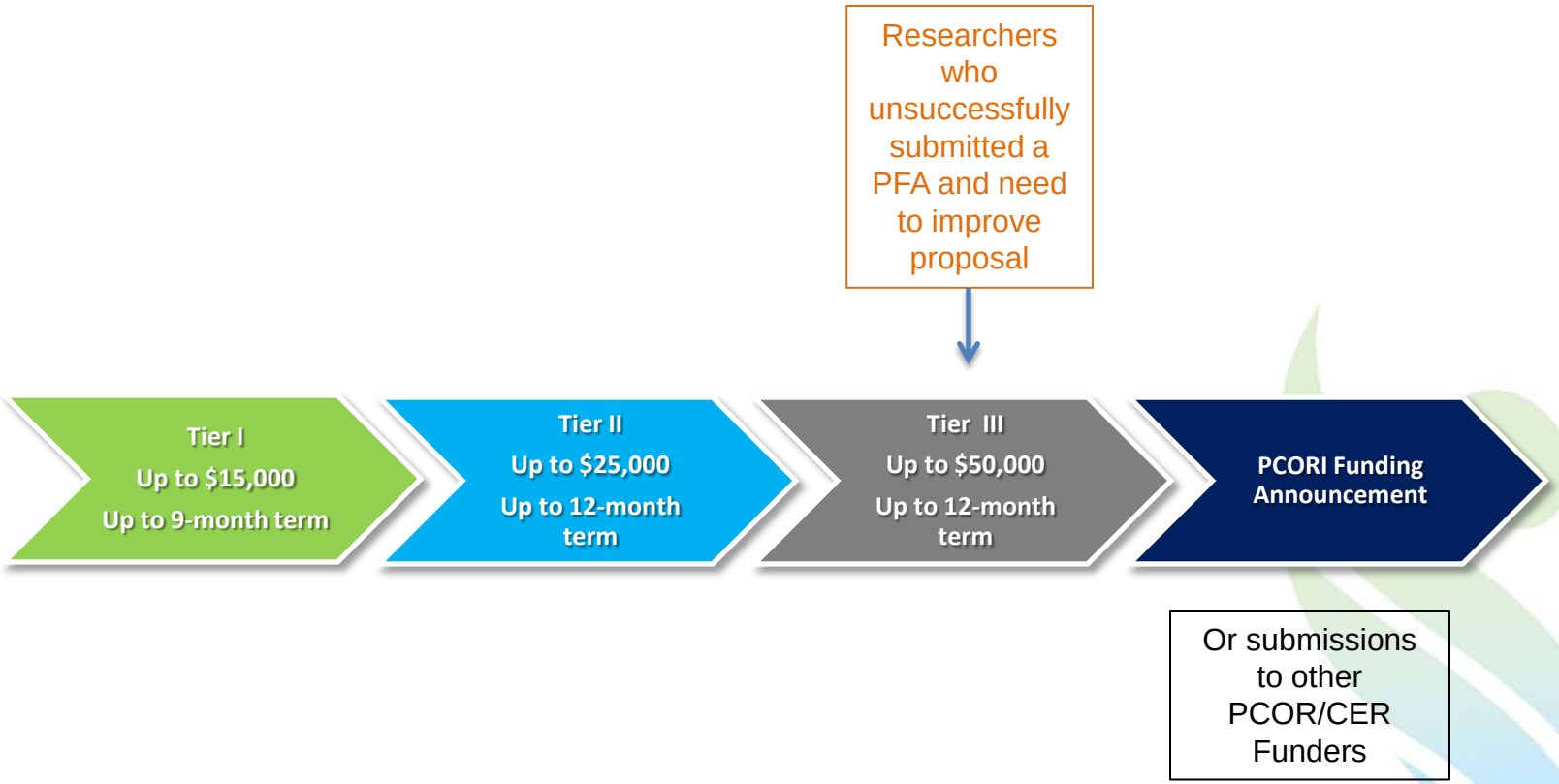
1) P2P helps foster capacity building for PCOR in the community before a study plan is even developed. This enables underserved/minority and otherwise "missing" communities to actively engage in the research process

2) It has been shown that when patient partners are engaged early on and throughout the research process, they are more likely to help in the implementation and dissemination of study results in their communities

Engagement and P2P Goals

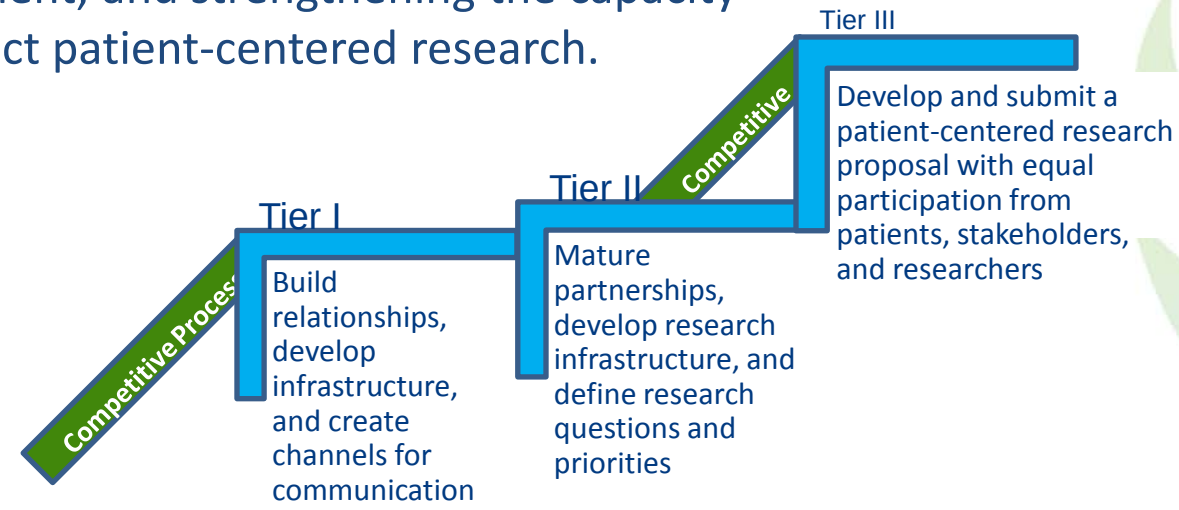


The Pipeline to Proposal Initiative Is Three-Tiered Award System



The Three Award Tiers

The three award tiers build on each other, with each successive step incrementally growing the community, increasing the levels of patient and stakeholder engagement, and strengthening the capacity to conduct patient-centered research.



Program/Awardee Management – Pipeline Award Program Offices

- PAPOs manage awardees in their region
- Managing awardees includes providing
  - technical assistance to ensure awardees can meet expectations,
  - handling all invoicing from awardees,
  - facilitating reporting from awardees, and assisting PCORI with evaluating awardees.
- PAPOs are also expected to work together to help improve the P2P program
- CFPHE provides consultation to PCORI, building on their past experience running the original P2P Cycle and other similar programs.

Regional Program Offices for Pipeline Awards

Michigan Public Health Institute

Colorado Foundation for Public Health and the Environment

National Network of Public Health Institutes

Health Resources in Action

Georgia Health Policy Center

Projects that cover more than one region are housed under the National Program Office

Program/Awardee Management – PCORI

- PCORI funds and manages the P2P program.
- PCORI evaluates PAPO work and compliance with their contracts.
- PCORI provides training for P2P Awardees
- PCORI evaluates reports submitted by PAPOs, including awardee activity reports

Review Process and Criteria for Tiers I & II

Tier I	Tier II
1. Program Fit - does this fit the spirit of the Pipeline to Proposal Awards? 2. Project Workplan and Timeline 3. Past Partnership or Community Engagement Experience 4. Budget/Cost Proposal Reviewers are External Reviewers with community engagement and/or research experience, PAPO Staff, Ambassadors, Merit Reviewers, and PCORI Staff	1. Adherence to Contract Requirements during the Tier I project period 2. Intent to continue Partnership Development 3. Responses to Final Report Reviewers are PCORI Staff and PAPO Staff

Pipeline to Proposal Awardees who enter at Tier I will have an opportunity to develop their patient/stakeholder/researcher partnership over a 21-month period.

How PCORI Evaluates the Program

- Reports
  - Awardee reports are a way for PCORI to evaluate the P2P program and the progress of the awardees
  - CFPHE has revised the monthly reporting form and created instructions on how to complete the form
- Process Improvement Surveys
  - These surveys are provided to determine the success of certain processes
  - Very soon, all reviewers will be sent a survey to provide their feedback on the full application review process.
  - We will provide you with these results once the survey is complete.
- LEAP Surveys
  - Learning About Partnerships (LEAP) Survey of awardees and partners
  - Other Methods of Evaluation
- Award tracking
  - Feedback from the Pipeline Awards Program Office via monthly reports
  - 12-month, 24-month, and 48-month follow-up with Pipeline to Proposal awardees (including the awardee and patient/stakeholder partners when applicable)

What We Hope to Learn from the P2P Program

- Are these investments successful in fostering partnerships?
- What are some elements of successful partnership structures?
- Did these partnerships embody the PCORI Engagement Principles?
- To what extent did this project prepare awardees to pursue research funding from PCORI or another funder?

What We Have Learned So Far…

- PCORI Engagement Principles are evident in the responses from the Final Reports (reciprocal relationships, co-learning, trust, honesty, partnership, transparency, and respect)
- Partnerships that are successful:
  - include diverse voices (e.g., community members and researchers; researchers of different types)
  - may contribute to individual and community empowerment
  - utilize the natural interests and shared passions across partners on the research topic
- Most projects that are prepared to move forward (to Tier II and/or other funding)
  - have specific plans for continued work
  - generate new ideas and/or increase the scope of their work
- Many respondents would like technical assistance and more networking through PCORI to complete their goals.
- Generally, respondents believe that PCORI funding has been influential and will have a lasting impact.

P2P Funded Rare Disease Projects

- Tier II
  - Cystic Life, Arizona, Project Lead – Ronnie Sharpe at CysticLife (West)
  - Addressing Obesity in Latino Adolescents with Spina Bifida/Supporting Latino Families with Children with Spina Bifida, California – Ruth Bush at Spina Bifida San Diego (West)
- Tier I
  - Bridging Rare Disease Patients and Data through Novel Research Partnerships, Indiana – Project Lead – Lisa Heral, RN at Parkview Health (National)
  - We'll Take the Village: Engaging the Community to Better Health – Mary Bentley LaMar, The Sickle Cell Association of New Jersey (East)
  - What's the SCOOP? Discovering Quality-of-Life Outcomes That Matter to Squamous Cell Carcinoma of the Oropharynx (SCOOP) Patients and Their Families, Project Lead Steven Chang , MD at Henry Ford Health System, (National)

CysticLife

- CysticLife is an active online community for patients with cystic fibrosis and their caregivers. Members exchange anecdotes regularly about what is working for them, what isn't, and the side effects they are experiencing. They believe that quantifying options for their community members so that they can make more informed decisions is an important next step, and have wanted to enable their community to conduct and participate in effectiveness research for quite some time. Further, they have envisioned how the community can collaborate on formulating the research question and then work with academic researchers and medical professionals in study design, management, and analysis.

Addressing Obesity in Latino Adolescents with Spina Bifida/Supporting Latino Families with Children with Spina Bifida

- This project focuses on providing a network for Latino families with children with spina bifida. Over the past few years, in response to feedback from parents and pediatric patients, Spina Bifida San Diego has recognized the need to address the weight issues facing our affected pediatric patients. They have created a network of patient and family stakeholders who are invested in identifying the obesity issues facing our predominantly Latino spina bifida population, through structured focus meetings facilitated by a nutritionist and a bilingual assistant. We are working with community investigators in obesity research to create a panel of patients, parents, caretakers, and researchers; those individuals provide the self-motivation, dedication, and meaningful solutions needed to address the prevention and resolution of obesity in this high-risk population.

Bridging Rare Disease Patients and Data through Novel Research Partnerships

- This project focuses on the rare disease fibrous dysplasia and related disorders associated with excess bone growth. The Tier I portion of the project will focus on building the community, which includes 1) forming new and strengthening existing research partnerships, and 2) creating appropriate communication and outreach plans to support collaboration among the advocacy and research organizations as well as patients, researchers, and clinicians. In building the appropriate online tools, partnerships, and governance structures, we will take the first steps toward improving patient-centered outcomes research for this rare disorder.

We'll Take the Village: Engaging the Community in Better Health

- This project proposes to engage our patients and others from the nontraditional research community in identifying areas they consider important for comparative research that will lead to increased use of medical and nonmedical resources for individuals affected by sickle cell disease (SCD) in New Jersey. They expect that this will ultimately lead to healthier outcomes and to reduced health disparities. This project will be guided by the voice of the patient.

What's the SCOOP? Discovering Quality-of-Life Outcomes that Matter to Squamous Cell Carcinoma of the Oropharynx (SCOOP) Patients and their Families

- This project will create a patient advisory council of head and neck cancer survivors and caregivers in Michigan, then expand virtually through the Cancer Research Network to provide input about the patient experience after these treatments. The council will identify short- and long-term outcomes that are important to them. In the next phase (Tier II), the project will engage the council in the development of comparative effectiveness research questions, proposing a pragmatic trial of treatment strategies (surgery versus radiation) in SCOOP patients.

Lunch

12:00 – 1:00 p.m.

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

CTAP Subcommittee on Recruitment, Accrual, and Retention

Margo Michaels, MPH
Founder, Education Network to Advance Cancer Clinical Trials
Advisory Panel on Clinical Trials, Member

Subcommittee on Recruitment, Accrual, and Retention (RAR)

- While research base is limited, there are key best practices in RAR that should be employed. The subcommittee will
  - inform PCORI Funding Announcements and related review criteria;
  - guide PCORI monitoring of funded contracts by providing technical assistance and support; and
  - provide additional direction regarding the engagement of healthcare stakeholders around recruitment, accrual and retention
- We will provide guidance to PCORI on topics relating to the recruitment, accrual, and retention of human subjects, research participants, including the enhancement of RAR for all groups, with a special focus on medically underserved populations.

Subcommittee on Recruitment, Accrual, and Retention (RAR)

- Given PCORI's mandate to improve the quality and relevance of evidence available to help people make informed healthcare decisions, we must ensure that the ***research PCORI produces is truly representative of the affected population(s) and that funded studies serve both the study participants and the study research question(s) by achieving all necessary recruitment, accrual, and retention targets.***

Areas of Exploration

- Methodology Standards
- Development of Letters of Intent/ Funding Announcements (PFAs)
- Engagement Expectations /Engagement Monitoring
- Merit Review/Merit Review Training
- Contract Negotiation /Information Requests
- Program and Engagement Officers Monitoring Funded Projects
- PCORNET

Subcommittee on Recruitment, Accrual, and Retention (RAR)

- **List of tasks/priorities for next 12-18 months**
  - Refine PCORI Methodology Standards on Patient-Centeredness to include definitions of and practices for “Patient-Centered Recruitment and Retention”
  - Provide technical assistance and support – ad hoc as needed by PCORI
    - Provide comments on new interim report template
    - Provide comments on Project Remediation SOP
    - Serve on Post-Award Advisory Subcommittee as recruitment and retention “experts”
  - Provide technical assistance and support – RAR tool kit for staff to monitor clinical trials
  - Advise on Scope of Work for contractor to develop a tool kit/guide to monitor projects

Subcommittee on Recruitment, Accrual, and Retention (RAR)

- **Members**
  - CTAP Members
    - Margo Michaels (chair)
    - Sanford Jeames
  - MC Member
    - David Meltzer
  - RDAP Member
    - Kate Lorig, DrPH
  - Outside Experts
    - Clair Meunier
    - Giselle Corbie-Smith, MD, MSc
    - Terrance Albrecht, PhD
    - Deborah Watkins Bruner, PhD, RN, FAAN
    - Consuelo Wilkins, MD, MSCI

Follow-up Analysis of Letters of Intent (LOIs) on Rare Diseases: Spring 2015 Cycle

Lauren Fayish, MPH
Program Associate, Evaluation & Analysis

Laura Forsythe, PhD, MPH
Associate Director, Evaluation & Analysis

Vadim Y. Gershteyn, MPH
Program Associate, Evaluation & Analysis

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

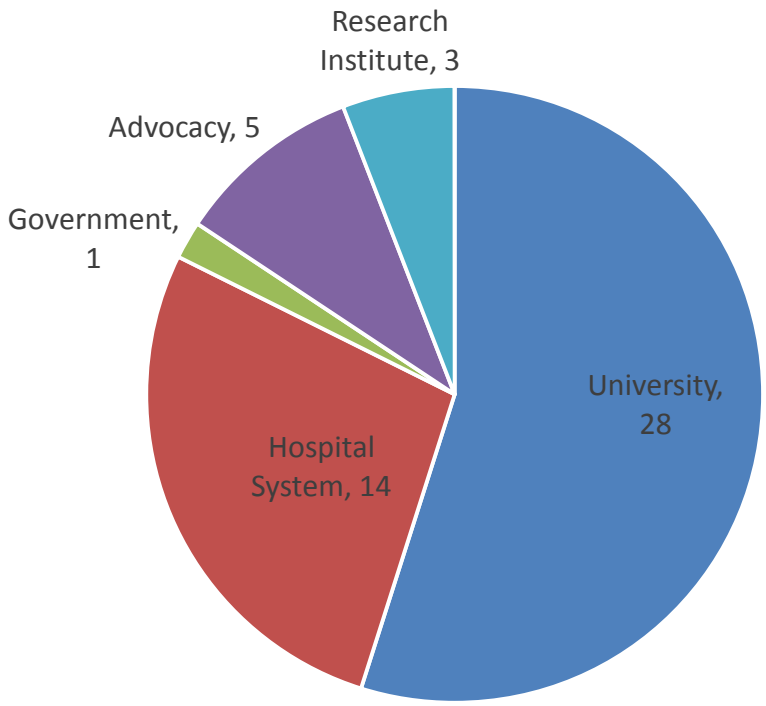
Funded Projects on Rare Disease

- Through April 2015, PCORI has 49 awards on Rare Diseases
  - 18 through Broad Funding Announcements (6%)
  - 3 Pilot Projects (6%)
  - 20 Networks (100% of Clinical Data Research Networks; 50% of Patient-Powered Research Networks)
  - 5 Pipeline to Proposal awards (6%)
  - 3 Engagement awards (8%)

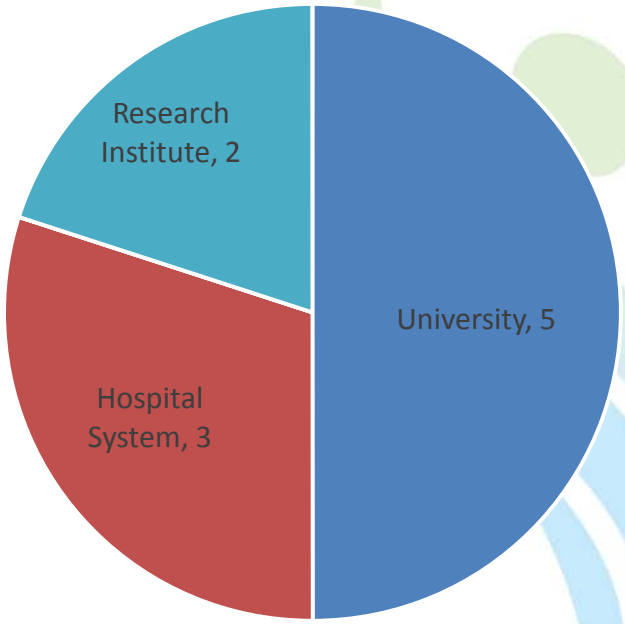
PI Institutional Affiliation† for Rare Disease Applicants in Broad Funding Announcements

Cycle III - Spring 2014

All Rare Disease Applicants (n=51)



Funded Rare Disease Applicants (n=10)



†PI self-reported

Evaluation of Applications on Rare Diseases

- RDAP presented PCORI with questions about Merit Review for applications on rare diseases
  - How many applications on rare diseases are reviewed, discussed, and funded compared to other conditions?
  - Compared to other applications, how likely are applications on rare diseases
    - to be discussed (i.e., part of the review slate at the in-person panels)? Why?
    - to be funded? Why?

Summary of Findings (presented Jan 2015)

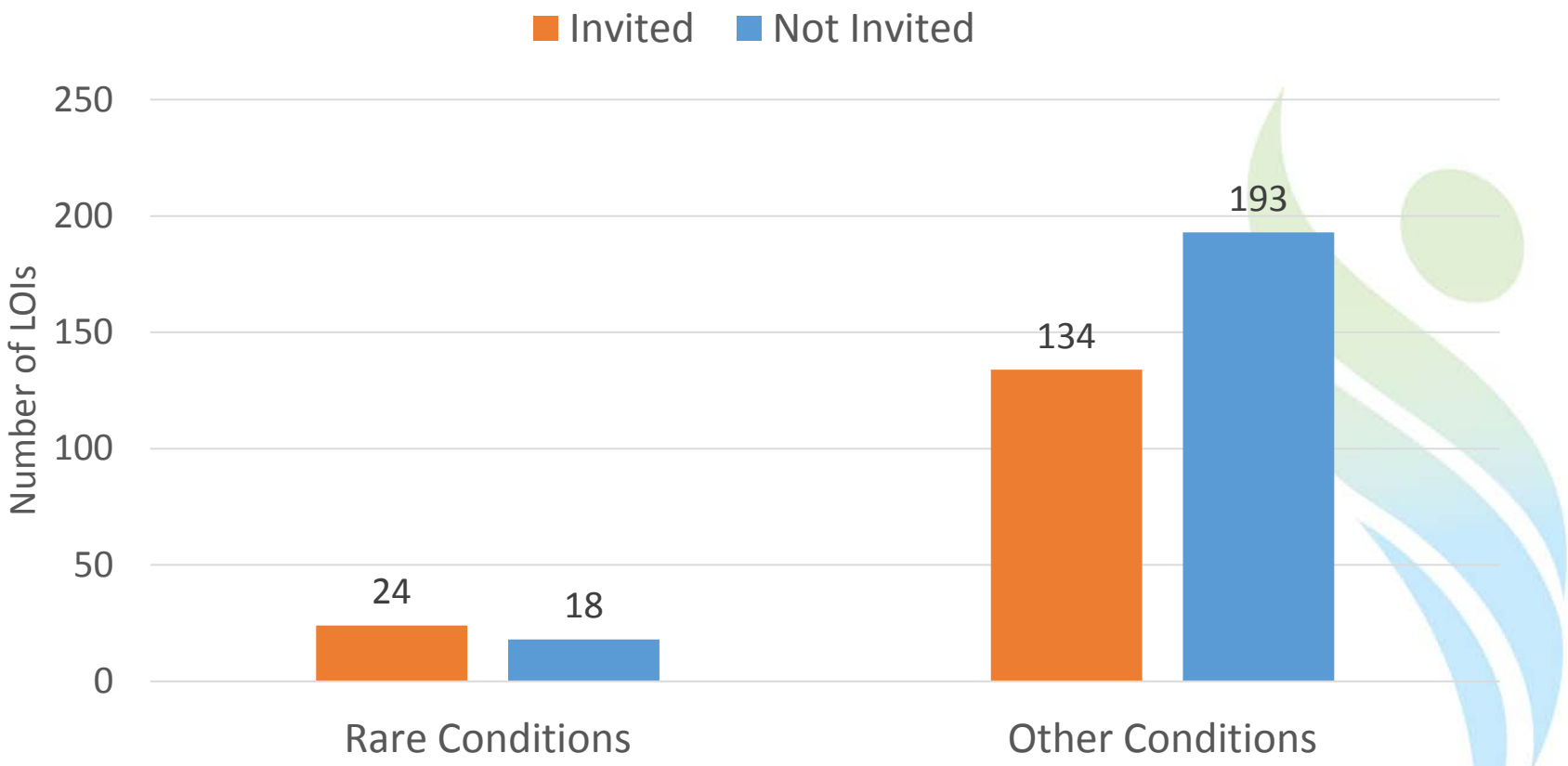
- Applications on rare diseases are not disadvantaged in PCORI Merit Review
  - More likely to be discussed at in-person panels
  - More likely to be funded
  - Score similarly or better on each criterion
- However, PCORI received a limited number of applications on rare diseases

Action Steps

- Set aside funding for rare disease research in the Spring 2015 PFA ($12 M)
- Applications on rare diseases will be reviewed in separate panel(s) to ensure relevant experts are included

Spring 2015 LOIs: Rare vs. Other Conditions

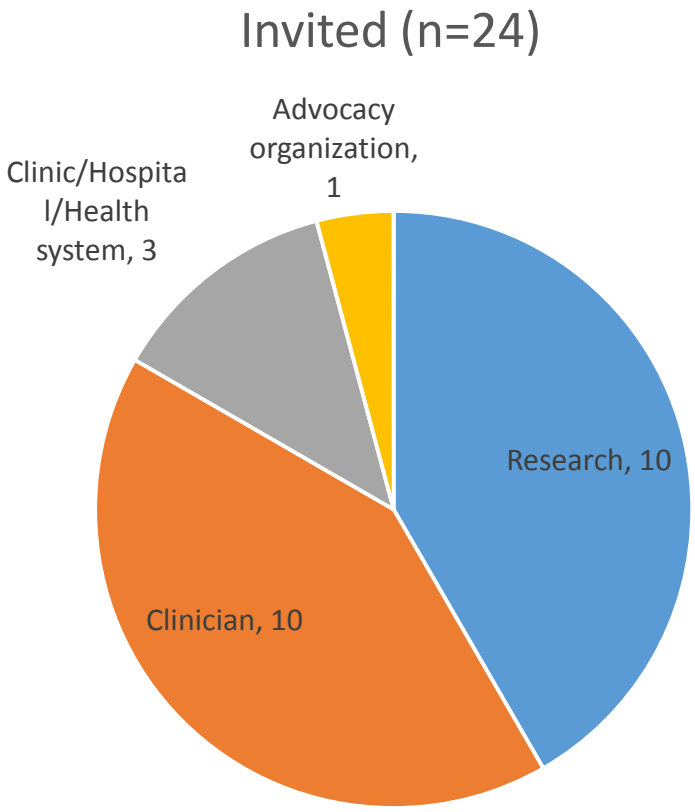
- **57% of LOIs on rare diseases invited vs. 41% of other LOIs**
- **LOIs on rare diseases account for 15% of all invited LOIs**

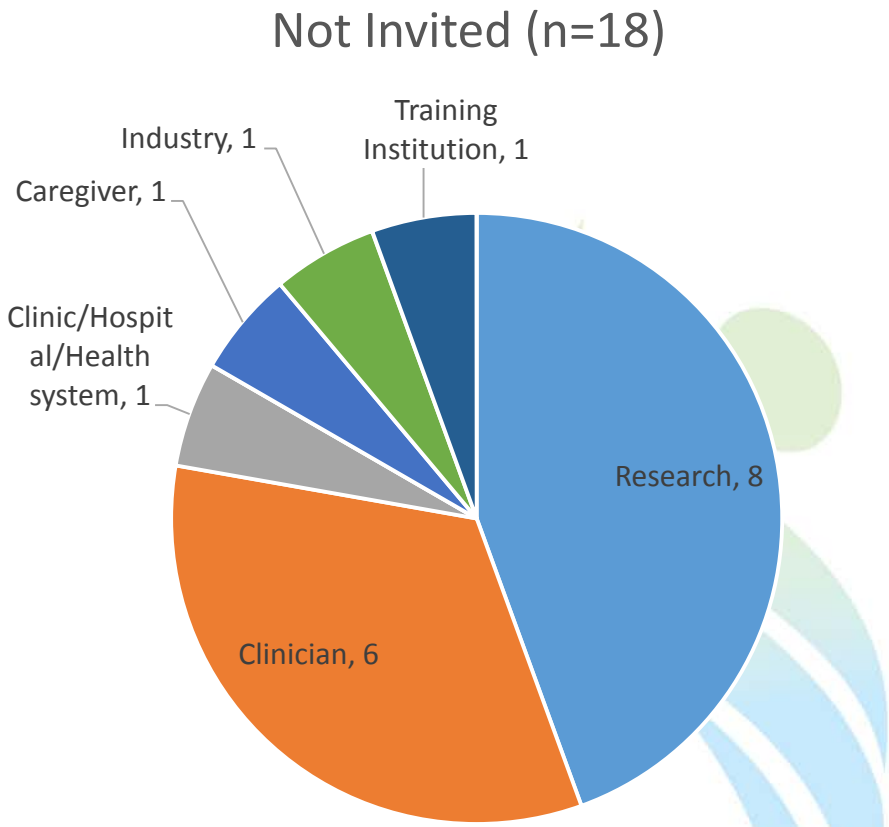


Purpose of LOI Analysis

- PCORI conducted an analysis of Letters of Intent (LOIs) on rare diseases to understand the characteristics of LOIs that were invited for a full application vs. those that were not invited

Principal Investigator Stakeholder Community†
LOIs on rare diseases



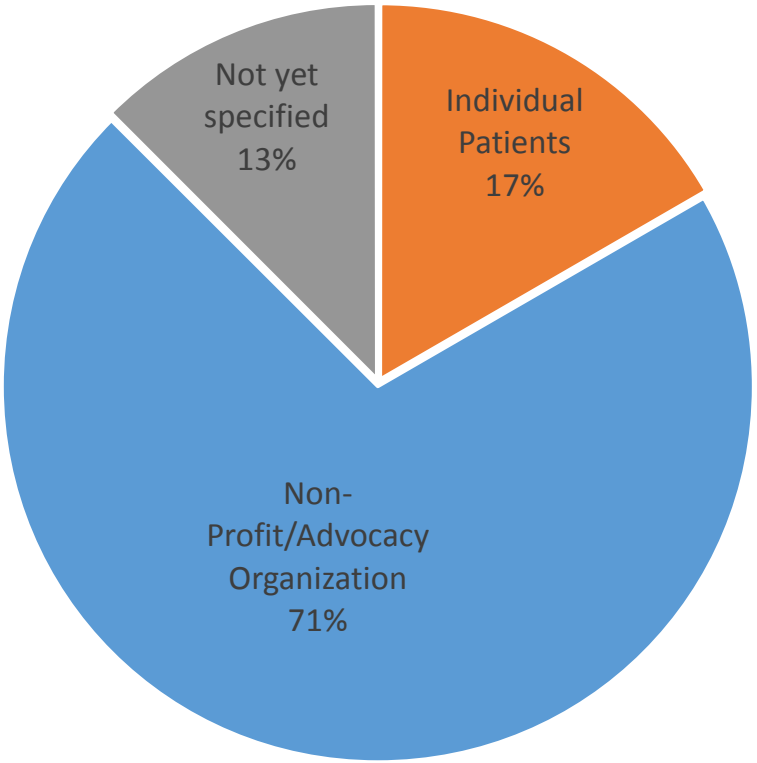


†PI self-reported

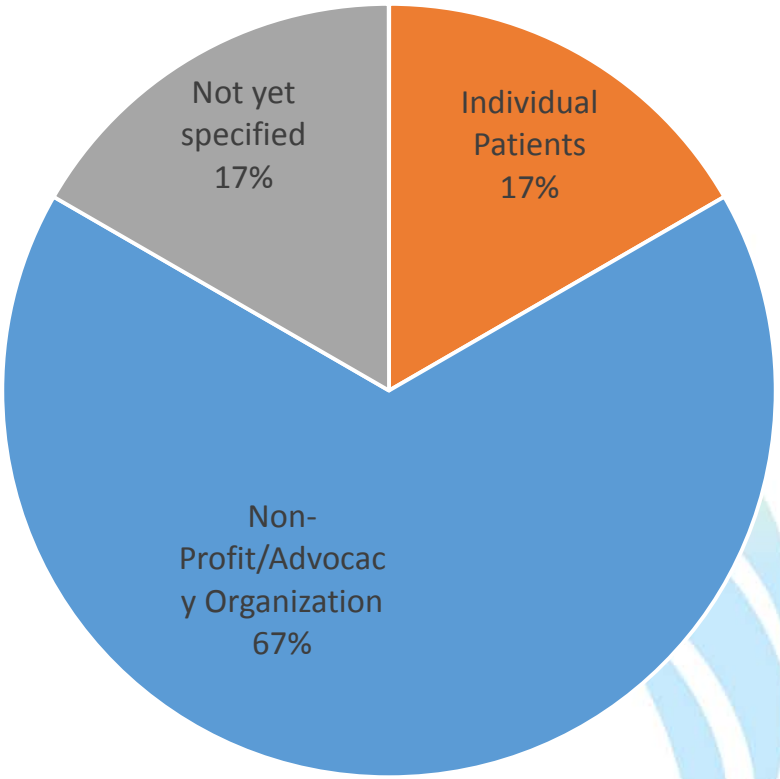
Patient-Stakeholder Partners

LOIs on rare diseases

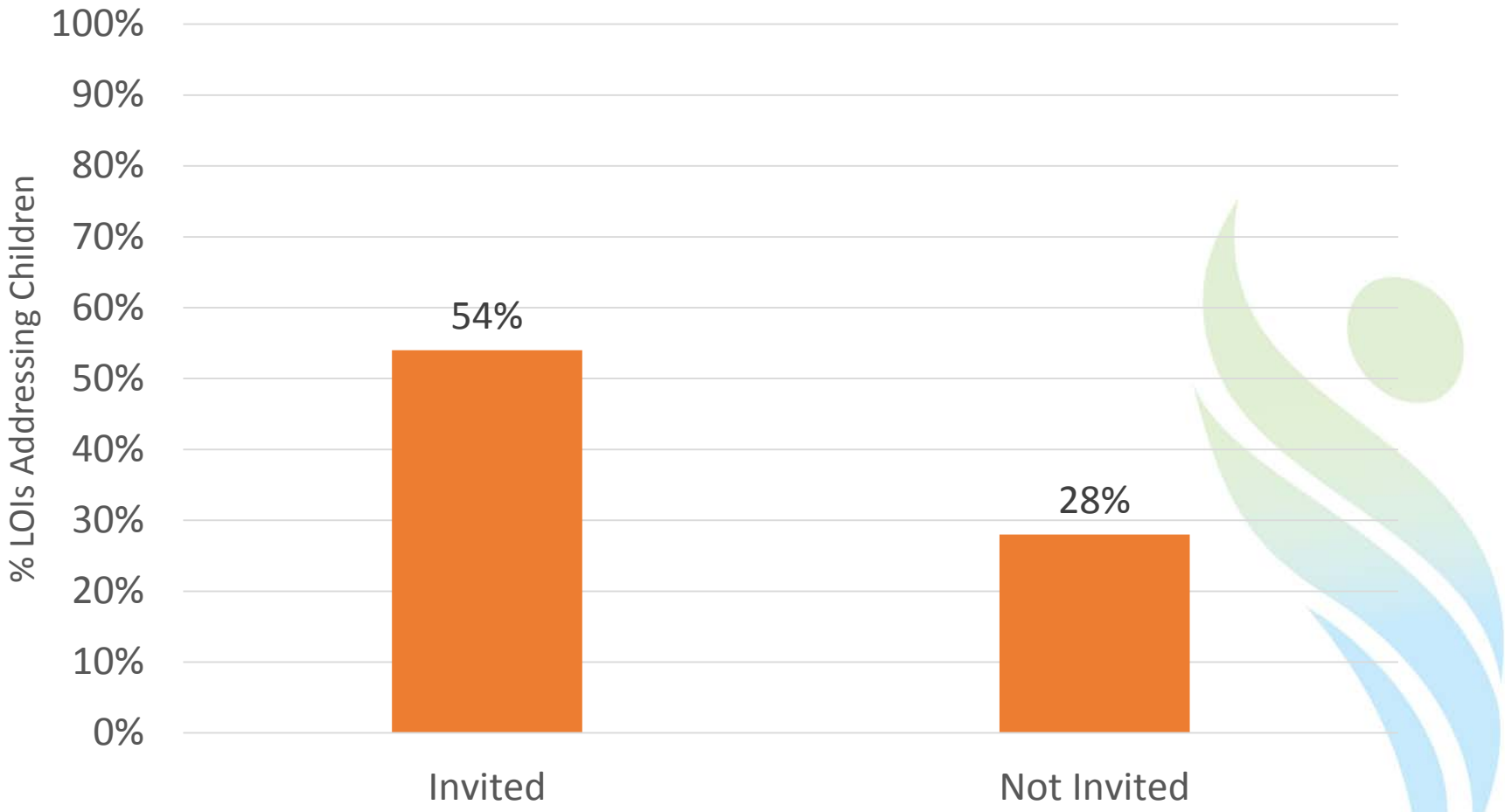
Invited (n=24)



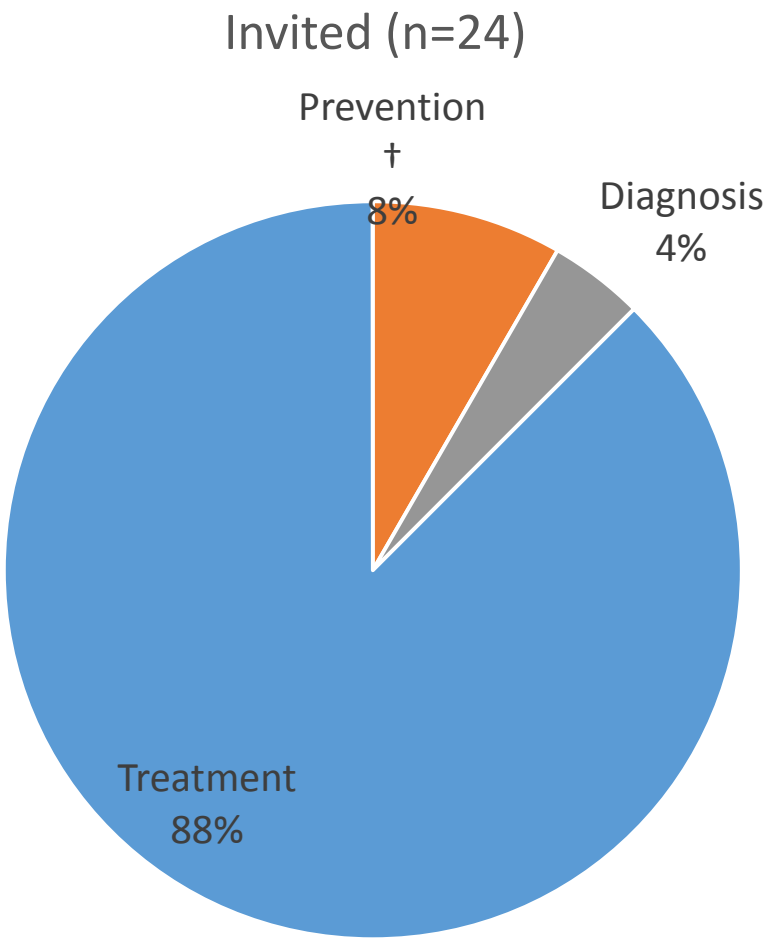
Not Invited (n=18)

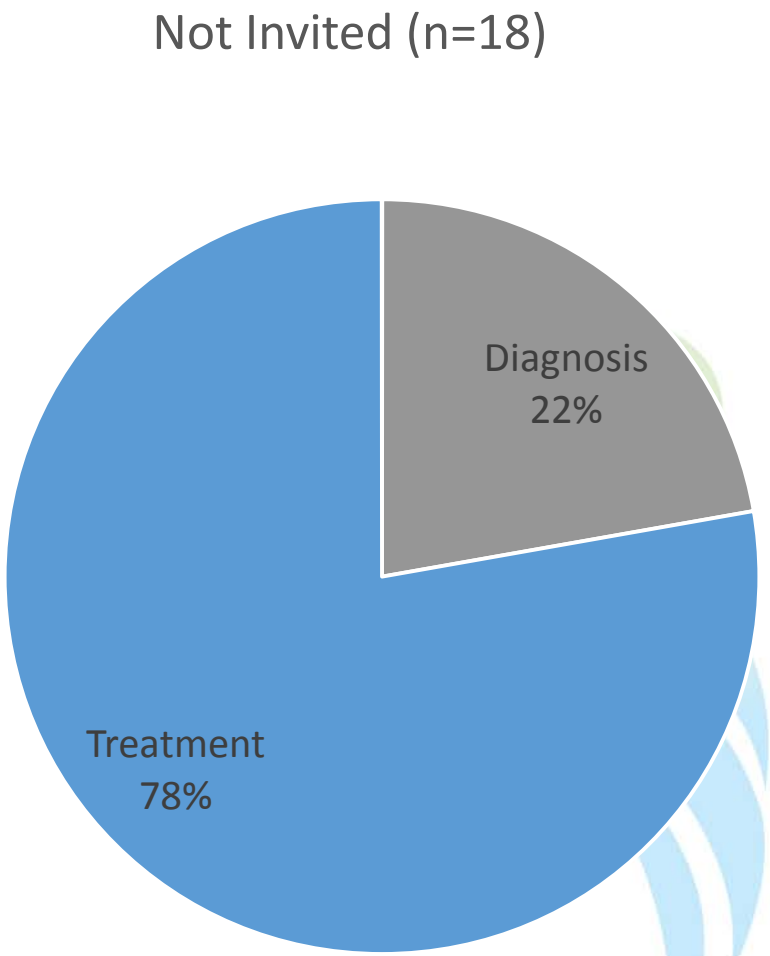


Pediatric Population Addressed
LOIs on rare diseases



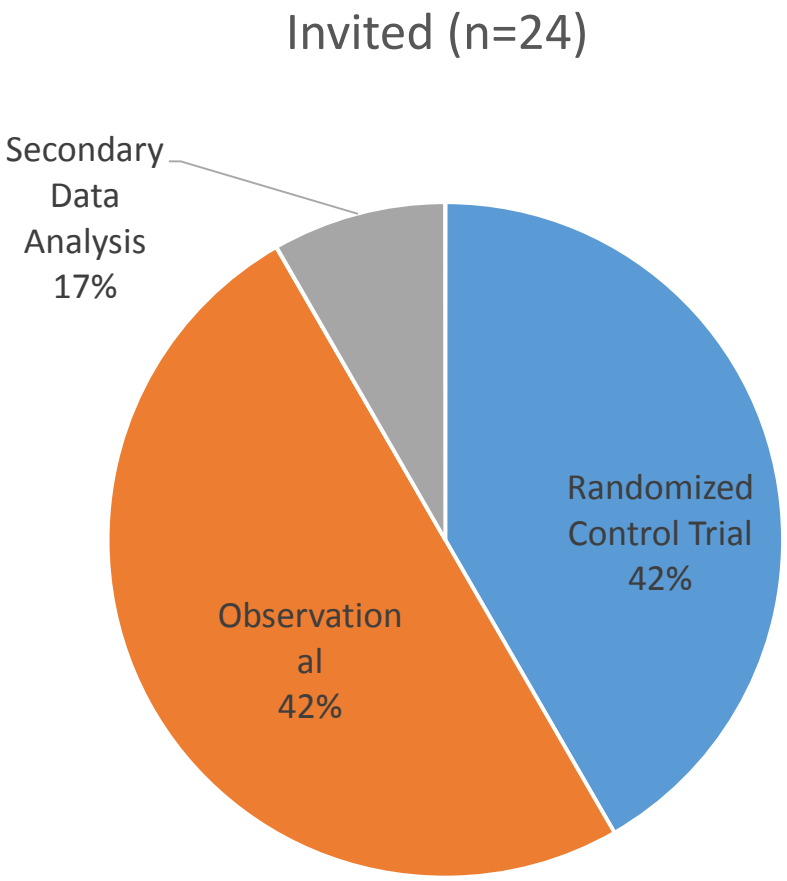
Care Continuum
LOIs on rare diseases

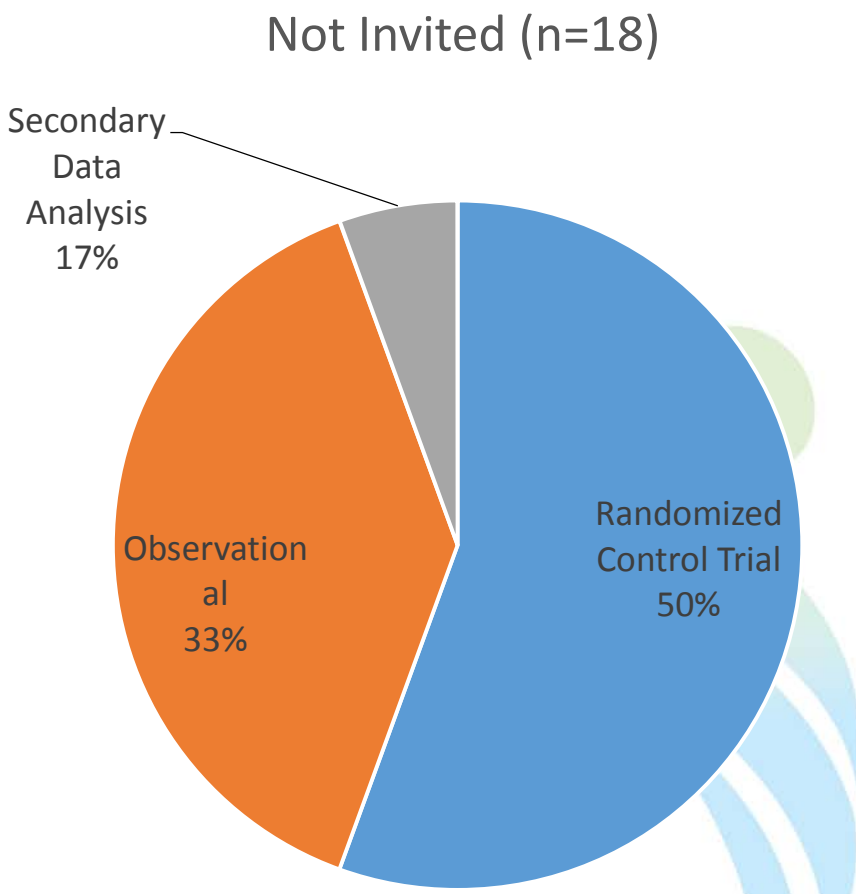




† includes one primary prevention LOI and one secondary prevention LOI

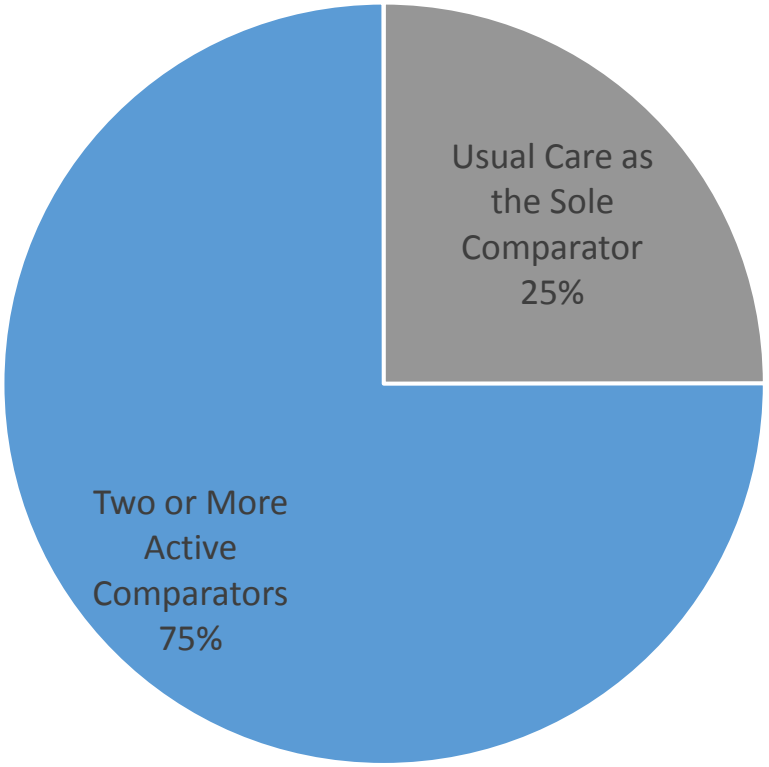
Study Design
LOIs on rare diseases



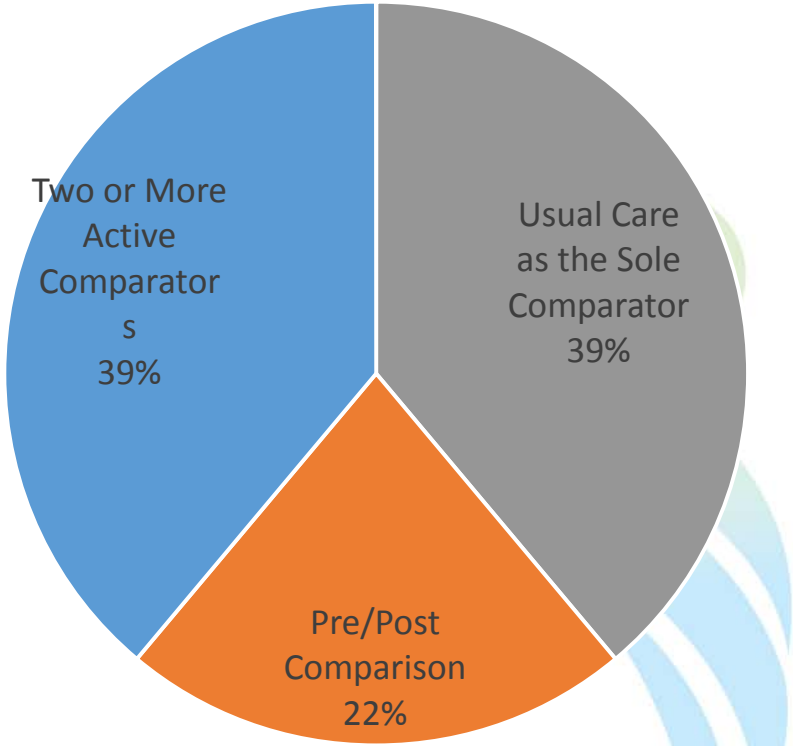


Comparators†
LOIs on rare diseases

Invited (n=24)



Not Invited (n=18)



†"Usual care" is PI-defined standard of care practice

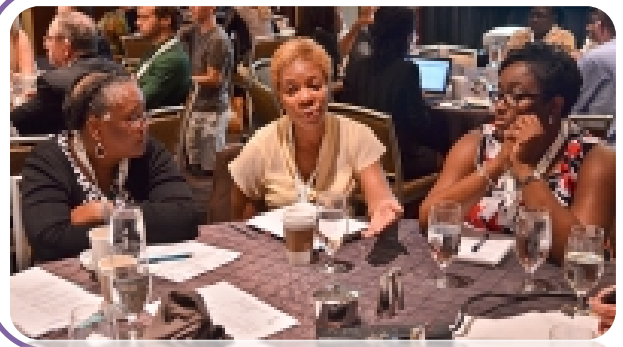
Thank You

Exploring the Eugene Washington PCORI Engagement Award Program

Lia Hotchkiss, MPH
Director, Eugene Washington Engagement Awards Program, PCORI

PCORI Engagement Goals

Build a patient-centered outcomes research (PCOR) community



Engage the PCOR community in research

Promote dissemination and implementation of PCOR research findings

Eugene Washington PCORI Engagement Award Program

- Launched in February 2014
- Provides support for projects that lead to better integration of patients and other stakeholders in the healthcare research process
- A programmatic funding opportunity – not research awards
- Program budget $15.5 million (FY 2015)
- Awards up to 2 years in duration; $250,000 total costs
- Fund awards through contracts rather than grants; PCORI programmatic involvement with awardees expected throughout the post-award process

Engagement Awards Intended to Support

- Engagement projects:

Knowledge Awards	Training & Development Awards	Dissemination Awards
• **Increase knowledge** about how consumers of healthcare information view, receive, and make use of PCOR and CER	• **Build capacity** for participating in PCOR and CER and create ways to connect patients, caregivers, and other stakeholders with the research community	• **Develop and strengthen channels** for disseminating and implementing PCOR and CER findings

- Meetings and conferences that align with PCORI's Mission and Strategic Plan* and facilitate expansion of PCOR/CER

*available at http://www.pcori.org/sites/default/files/PCORI-Board-Meeting-Strategic-Plan-111813.pdf

Our Growing Engagement Award Portfolio

- Projects focus on a variety of PCORI stakeholder groups: patients, caregivers, advocacy organizations, clinicians, hospitals and health systems, researchers, policy makers, payers
- Will produce deliverables that are useful to awardees, PCORI, and the broader PCOR community for increasing patient and stakeholder engagement in PCOR and CER
- We are committed to sharing and using this information
- Project abstracts available at http://www.pcori.org/research-results

Anticipated Project Deliverables

Network of individuals living with sickle cell disease who are prepared to take part in PCOR

Educational program on PCOR specifically for staff, patients, and caregivers of rare disease organizations

Training for community partners to engage in projects to address issues faced by ethnically diverse and under-resourced seniors as they try to age in place

Meeting with researchers and patients to develop a vision, mission, and research priorities for the nontuberculous mycobacterium research consortium

Anticipated Project Deliverables

Landscape review of programs used by policy makers to leverage PCOR and CER, and a roadmap to guide them in the use of PCOR and CER

Enhanced year-long training curriculum designed to educate and engage health center teams—including patients and clinical and administrative staff—in PCOR

Openly accessible, web-based portal with resources about engagement for both patients and researchers

Model for effective engagement of patients and community members in construction of Community Hospital Needs Assessments and effective review and integration of PCOR

Anticipated Project Deliverables

Conference to explore opportunities and strategies for overcoming obstacles in dissemination and implementation research and a summary of the proceedings

Sustainable method for conducting research prioritization with bladder cancer patients on an iterative and ongoing basis

Network to connect parents of children with medical complexity to each other and to their key healthcare providers to identify the most common challenges they face in the healthcare continuum

Conference summary that defines the academic approaches to PCOR and CER training

Engagement Awards Not Intended to Support

- Research projects
- Planning/pilot studies
- Demonstration projects
- Evaluations of programs or interventions
- Validation of tools or instruments
- Delivery of health care
- Development of registries
- Recruitment of study subjects or activities to increase participation in registries
- Development of decision aids or clinical practice guidelines
- Career development awards
- Meetings that are business as usual, without focus on PCOR or CER

Our Application Process

Who Can Apply

- Private Sector
  - Nonprofit and for-profit research organizations
- Public Sector
  - Universities and colleges; hospitals and healthcare systems; laboratories and manufacturers; units of state, local, or federal government.
- US Organizations
  - Must be recognized by the Internal Revenue Service
- Foreign Organizations and Nondomestic Components of US Organizations
  - May apply if here is demonstrable benefit to the US healthcare system; US efforts in the area of patient-centered research can be clearly shown
- Individuals
  - Not permitted to apply

How to Submit

- http://www.pcori.org/funding/opportunities

Engagement Award (EAIN): Research Meeting and Conference Support

Key Deadlines	Type	Funds Available	Total Costs
LOI: Not required **Application:** July 1, 2015	Program Award		One-time award total costs must not exceed $50,000 and multi-year award total costs may not exceed $250,000.

Engagement Award: Knowledge, Training and Development, and Dissemination Awards

Key Deadlines	Type	Funds Available	Total Costs
LOI: July 1, 2015 **Application:** Full proposals are due 40 days after review and approval of the LOI.	Program Award		Award total costs may not exceed $250,000

What to Submit

Letter of Inquiry	
Organization and Project Lead Information	
Project Information (Project Summary)	
Application	
Organization and Project Lead Information	
Project Information	
Key Personnel	
Collaboration and Partnerships	
Board of Directors List	Upload
Project Workplan and Timeline	Upload
Budget Summary	Upload
Budget Justification	Upload
Professional Profile/Biosketch	Upload
Letters of Support	Upload Optional
Recent Articles/Evaluations	Upload Optional

Engagement Award applicant resources including online application system user manuals for submitting LOIs and full proposals available on PCORI website

Review Process

- If applying for meeting/conference support, you do not need to submit an LOI. Applicants proceed directly to submitting a full proposal.
- In FY2015, LOIs and proposals for meeting/conference support are accepted on an ongoing basis, but reviewed quarterly beginning on October 1, January 2, April 1, and **July 1**.
- Applications are reviewed by at least 3 members of PCORI's Engagement Team, Contracts Management and Administration, and other internal staff, as needed.

Merit Review Criteria

- Program Fit
- Project Plan and Timeline
- Qualifications of the Project Lead, Personnel, and Organization
- Patient and Stakeholder Engagement Plan and Collaborations
- Past Performance
- Budget/Cost Proposal

Is there adequate engagement of patients and other stakeholders in the design and conduct of the proposed project?
Are collaborations meaningful and appropriate based on aligning the interest, expertise, and scope of work of each member of the team and the collaborators involved?

Allowable vs. Unallowable Costs

For More Information

Quick Links for Applicants

Key Terms Glossary

Frequently Asked Questions (FAQs)

PCORI Online User Manual: Start a LOI

PCORI Online User Manual: Submitting an Application

PCORI Funded Projects: Sample Engagement Plans

Visit

pcori.org/eugene-washington-awards

Contact us at

- ea@pcori.org
- 202-370-9312

Thank You

Potential Uses for Chatter

Emma Djabali

Program Associate, Office of the Chief Science Officer, PCORI

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Recap and Next Steps

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI
Marshall L. Summar, MD
Chair, Advisory Panel on Rare Disease, PCORI
Vincent Del Gaizo
Co-Chair, Advisory Panel on Rare Disease, PCORI

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