Advisory Panel on Rare Disease Spring 2014 Meeting

Alexandria, VA

April 30, 2014 – 8:30 a.m. to 5:30 p.m. EST

Patient-Centered Outcomes Research Institute

Welcome and Plans for the Day

Joe V. Selby, MD, MPH
Executive Director, PCORI

Patient-Centered Outcomes Research Institute

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.

Today's Agenda

Start Time	Item	Speaker
8:30 a.m.	Conflict of Interest Disclosures	J. Selby
8:45 a.m.	Roles & Goals of Panel	B. Luce
9:15 a.m.	Rare Disease Roundtable Report	G. Martin
10:00 a.m.	PCORI's Rare Disease Portfolio and Plans	S. Ip R. Fleurence
12:00 p.m.	Lunch	
1:00 p.m.	Open Discussions	B. Luce
4:15 p.m.	Organizational Issues	B. Luce
5:00 p.m.	Post-Event Survey	
5:15 p.m.	Recap and Next Steps	B. Luce
5:30 p.m.	Adjourn	

Meeting Objectives

- Introduce PCORI staff & RDAP panelists
- Clarify panel roles & objectives
- Introduce PCORI's rare disease research portfolio
- Agree on panel's scope of work
- Discuss organization issues, including leadership

Conflicts of Interest

Joe V. Selby, MD, MPH
Executive Director, PCORI

Patient-Centered Outcomes Research Institute

Why is COI Important?

- PCORI has a legal obligation to publicly disclose conflict of interest statements for members of the Board, Methodology Committee, Advisory Panels and executive staff as well as in an annual report to Congress and the President.

- Transparency is important because it gives the public information about backgrounds and relationships that may inform actions.

What should you disclose?

- If you have financial or personal relationships that may have the potential to bias or have the appearance of biasing your decisions, you should disclose them.

Disclose, for example:

  - Employment
  - Financial income, such as stock, honoraria, consulting fees, etc.
  - Memberships/Leadership positions in other health care organizations
- Disclose as it relates to yourself, your spouse, domestic partner, children, parents, and others indicated.

Conflict of Interest Session

Next Steps

Each panel has a few minutes on their agenda for each panelist to fill out a COI disclosure form.

We will provide you with guidelines and formatting, and Staff will be available to answer any questions you may have about filling out the COI disclosure form.

Questions?

Roles and Goals of the Advisory Panel on Rare Disease

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI

Patient-Centered Outcomes Research Institute

Charter – Purpose

The Advisory Panel on Rare Disease will provide recommendations regarding the conduct of patient-centered CER in rare diseases to PCORI's:

- Board of Governors
- Methodology Committee
- Staff

Note: The RD Panel will not serve in an official decision-making capacity.

Charter of the Advisory Panel on Rare Disease – Approved by PCORI Board of Governors – November 18, 2013

Charter – Scope of Work

The Advisory Panel on Rare Disease will provide recommendations regarding:

- Research needs
- Conduct of research
- Infrastructure (data sources, tools)
- Experts for ad hoc panels (e.g. for specific research topics)
- Evaluating/disseminating PCORI's rare diseases research portfolio
- Targets and strategies for dissemination effort
- Collaboration opportunities with existing international, federal, public and private entities doing similar work in the rare disease space
- How other PCORI committees and panels should address unique considerations of rare disease

Charter of the Advisory Panel on Rare Disease – Approved by PCORI Board of Governors – November 18, 2013

Ad Hoc Expert Advisory Panels

In the case of a research study for each rare disease, the RD Panel shall assist PCORI in identifying experts to serve on a condition-specific ad hoc advisory panel to assist in:

- Evaluating
- Designing
- Conducting
- Determining the relative value and feasibility of conducting the research study

The chair of the RD panel will appoint members from:

- The RD panel
- Other individuals with appropriate expertise in the rare disease to be studied

Charter of the Advisory Panel on Rare Disease – Approved by PCORI Board of Governors – November 18, 2013

PCORI's Rare Disease Roundtable

Greg Martin
Deputy Director, Stakeholder Engagement, PCORI

Patient-Centered Outcomes Research Institute

Roundtable Objectives

- Discuss the relevant issues of the rare diseases community that could be addressed by PCORI's CER agenda
- Identify optimal strategies for engaging patients and other stakeholders in research on rare diseases
- Obtain feedback on PCORI's draft charter for a Rare Diseases Advisory Panel

Roundtable Discussion

- What are the relevant issues of the rare diseases community that could be addressed by a CER agenda?
  - Fostering earlier diagnosis and treatment in persons with symptoms
  - Evaluation of currently used off-label treatments
  - Comparative effectiveness studies of aggressive approaches
- How do PCORI and CER fit into the broader national research agenda?
  - Anne Pariser, MD, Associate Director for Rare Diseases, Food and Drug Administration
  - Cristina Csimma, PharmD, MHP, Chief Executive Officer, Cydan Development, Inc.

Discussion: Data Infrastructure

- Many rare diseases do not have registry.
  - Strong interest in creating registries
  - Some are supported for a brief period by NIH/ORDR
    - These registries wither when funding dries up.
    - Financial assistance needed for creation and maintenance of registries
    - Clear, consistent requirements, guidelines, methodology to ensure interoperability of data needed
- Consideration should be given to facilitating the identification of rare diseases in EMRs.
  - Data infrastructure needs to take into account patients as they transition from childhood to adulthood.
- **Roundtable Advice:**
  - *Collaborate with other agencies (FDA, NIH, etc.) on registry development.*

Discussion: International Cooperation

- Due to small sample sizes for many rare disease trials and studies, research usually requires international data sets.
- **Roundtable Advice:**
  - *PCORI should explore international collaborations when and where possible to facilitate effective research.*

Discussion: Treatment Options

- Only a small proportion of rare diseases have treatments
- Comparative clinical effectiveness of pharmaceutical options is challenging due to the limited number of drugs on the market.
- **Roundtable Advice:**
  - *PCORI's research should try to identify not only which drugs are effective but also the circumstances under which they are most effective.*

Discussion: Off-Label Treatments

- Much off-label usage of drugs exists for RD.
  - On occasions when a drug is taken off the market, those who use it off-label are left scrambling.
- When a drug is developed for a rare disease and other diseases find out that it works for them, rare disease patients can get left out
- **Roundtable Advice:**
  - *PCORI's work should not aim to have these uses added to the label but provide enough information so that patient and clinician are informed.*

Discussion: Ethics and Clinical Trials

- PCORI must also consider ethics in rare diseases research.
  - How should informed consent work within rare diseases research?
  - Should there be “clinical trials navigators” to help rare diseases patients understand risks?
  - Comparators other than “no treatment” are needed in order for it to be ethical to include RD patients in RCTs.

Discussion: Other Topics

- Significant rare disease care coordination questions exist, including:
  - Geographic dispersal, methods for dissemination of information among limited numbers of patients, and fostering patient engagement
- Discussion occasionally turned to areas outside of PCORI's remit:
  - Cost-effectiveness analysis
  - Clinical and coverage guidelines
  - Policy recommendations

Recommendations to PCORI

- Avoid “reinventing the wheel” on RD.
  - Wisely build upon the foundational work of many others.
- Consider research into rare diseases a model for research into personalized medicine.
  - Lessons learned from comparative clinical effectiveness research around rare diseases may be applicable to other rare or common conditions.
- Develop rules for aggregation of rare diseases or patients into clusters.
- Develop a catalog of rare diseases, or rare diseases issues, requiring CER/PCOR.
- Support data infrastructure in rare diseases.

Break

9:45 – 10:00 a.m. EST

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PCORI's Rare Disease Portfolio and Plans

Stanley Ip, MD
Senior Program Officer
Clinical Effectiveness Program

Rachael Fleurence, PhD
Program Director
CER Methods and Infrastructure Program

Patient-Centered Outcomes Research Institute

Summary of PCORI's Rare Disease Portfolio

- Number of PCORI-funded rare disease research projects: 8 as of January 2014
- Rare diseases included in our portfolio:
  - Alpha-1 antitrypsin deficiency (AATD, Alpha-1)
  - Vasculitis
  - Multiple sclerosis
  - Nephrotic syndrome
  - Pulmonary fibrosis
  - Myelitis
  - Sickle cell disease

Highlighted Projects

- A BioScreen for Multiple Sclerosis

  Principal Investigator: Stephen Hauser, MD

- Patient Participation Program for Pulmonary Fibrosis: Assessing the Effects of Supplemental Oxygen

  Principal Investigator: Jeffrey Swigris, DO, MS

- Comparative Effectiveness of a Decision Aid for Therapeutic Options in Sickle Cell Disease

  Principal Investigator: Lakshmanan Krishnamurti, MD

A BioScreen for Multiple Sclerosis

Engagement

- Patients and an advisory committee are engaged in the development and launch of a tool

Potential Impact

- Could influence practice by creating the first generation of a tool dedicated to personalized medicine in chronic diseases

Methods

- Iterative development, application analytics and surveys, and semi-directed interviews

Project Aim

Develops a digital portal to access and display real-time clinical information for use by multiple sclerosis patients and providers to improve treatment and decision making.

Stephen Hauser, MD,
University of California, San Francisco

PCORI Pilot Projects, awarded April 2012

A BioScreen for Multiple Sclerosis

"This ability to see their personal data compared to others has made our patients feel more engaged and empowered."

Pierre-Antoine Gourraud, PhD, MPH, Co-Investigator

Patient Participation Program for Pulmonary Fibrosis: Assessing the Effects of Supplemental Oxygen

Engagement

- Stakeholders will be involved throughout all planning phases of the project and will interview patients with pulmonary fibrosis

Potential Impact

- Could change practice by improving patient knowledge and understanding of symptoms, quality of life, and activity levels after the supplemental oxygen is prescribed

Methods

- Observational research

Collects data from pulmonary fibrosis patients who use O2, many of whom know little about its effects, to compare outcomes in order to make patients and prescribers more knowledgeable about possible effects.

Jeffrey Swigris, DO, MS,
National Jewish Health
Denver, CO

Assessment of Prevention, Diagnosis, and Treatment Options, awarded May 2013

Comparative Effectiveness of a Decision Aid for Therapeutic Options in Sickle Cell Disease

Engagement

- The development team for the decision aid will include a physician, behavioral scientist, and parent of a child with sickle cell disease

Potential Impact

- Could change practice by providing a more accurate perception of risks and benefits of treatment options for the 100,000 Americans with the disease

Methods

- Mixed methods and a randomized controlled trial

Develops and tests a web-based decision aid tailored to individual characteristics for patients with sickle cell disease. Key outcomes include patient knowledge, patient involvement in decision making, and decisional conflict and quality.

Lakshmanan Krishnamurti, MD,
University of Pittsburgh at Pittsburgh
Pittsburgh, PA

Assessment of Prevention, Diagnosis, and Treatment Options, awarded May 2013

Introducing PCORnet:
The National Patient-Centered Clinical Research Network

Rachael Fleurence, PhD
Program Director
CER Methods and Infrastructure Program

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The National Patient-Centered Clinical Research Network

This slide presentation explains:

- **Why** PCORnet was created
- **What** PCORnet will do for research
- **How** it works
- **Who** is involved

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Our national clinical research system is well-intentioned but flawed

- High percentage of decisions not supported by evidence*
- Health outcomes and disparities are not improving
- Current system is great **except**:
  - Too slow
  - Too expensive
  - Unreliable
  - Doesn't answer questions that matter most to patients
  - Unattractive to clinicians & administrators

We are not generating the evidence we need to support the healthcare decisions that patients and their doctors have to make every day.

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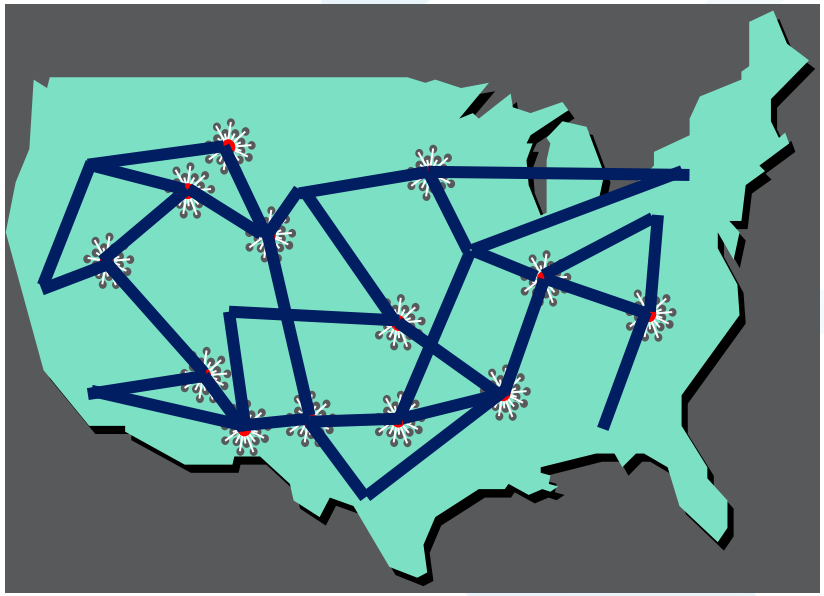
**Tricoci P et al. JAMA 2009;301:831-41.*

Both researchers and funders now recognize the value in integrating clinical research networks

- Linking existing networks means clinical research can be conducted more effectively
- Ensures that patients, providers, and scientists form true “communities of research”
- Creates “interoperability” – networks can share sites and data



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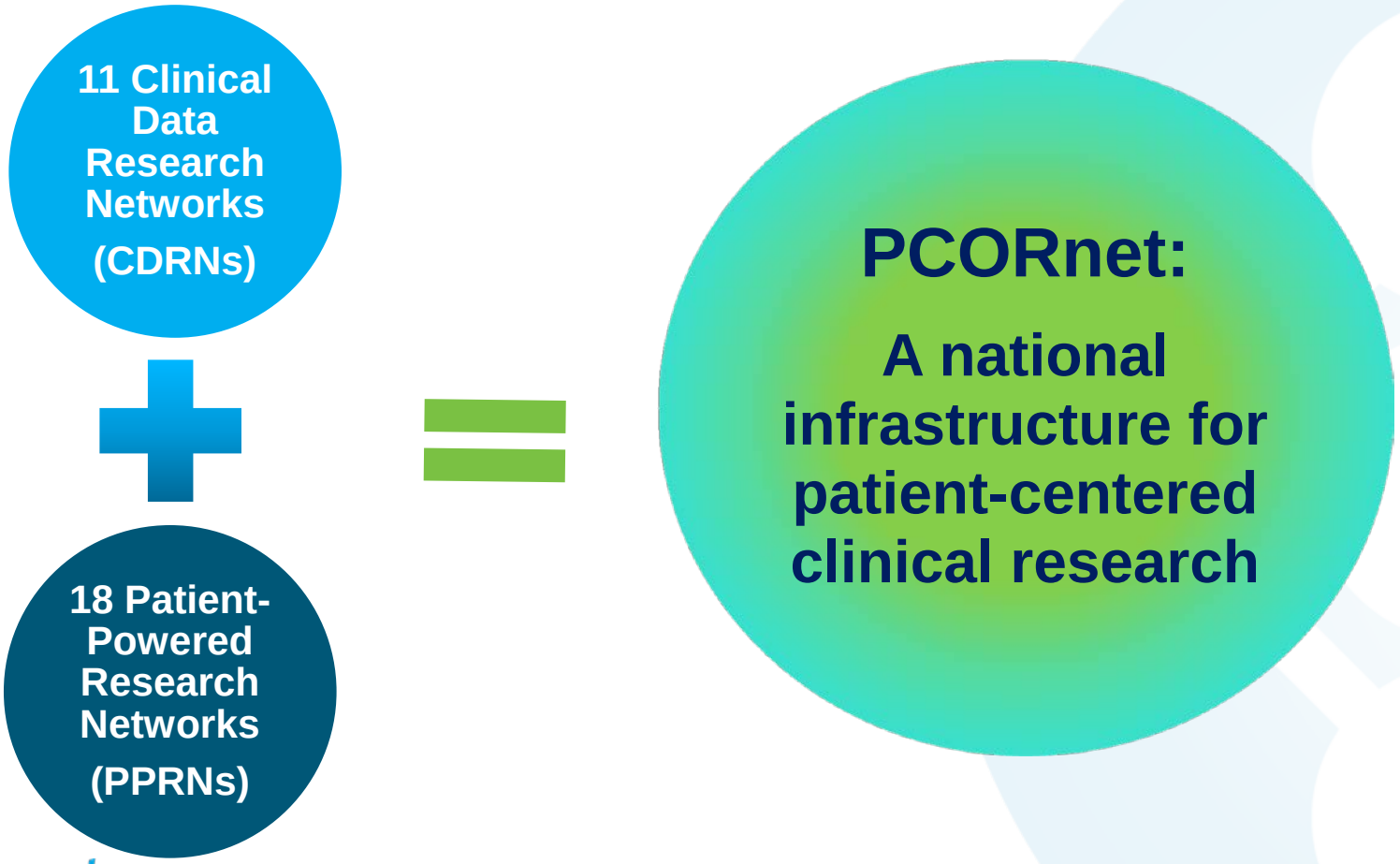
PCORnet embodies a “community of research” by uniting systems, patients & clinicians



What will PCORnet do for research?

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The National Patient-Centered Clinical Research Network

PCORnet's goal

PCORnet seeks to improve the nation's capacity to conduct clinical research by creating a large, highly representative, national patient-centered network that supports more efficient clinical trials and observational studies.

PCORnet's vision

PCORnet will support widespread capability for the US healthcare system to learn from research, meaning that large-scale research can be conducted with greater speed and accuracy within real-world care delivery systems.

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Overall objectives of PCORnet: achieving a single functional research network

- **Create** a secure national research resource that will enable teams of health researchers, patients, and their partners to work together on researching questions of shared interest.
- **Utilize** multiple rich data sources to support research, such as electronic health records, insurance claims data, and data reported directly by patients
- **Engage** patients, clinicians & health system leaders throughout the research cycle from idea generation to implementation
- **Support** observational and interventional research studies that compare how well different treatment options work for different people
- **Enable** external partners to collaborate with PCORI-funded networks
- **Sustain** PCORnet resources for a range of research activities supported by PCORI and other sponsors

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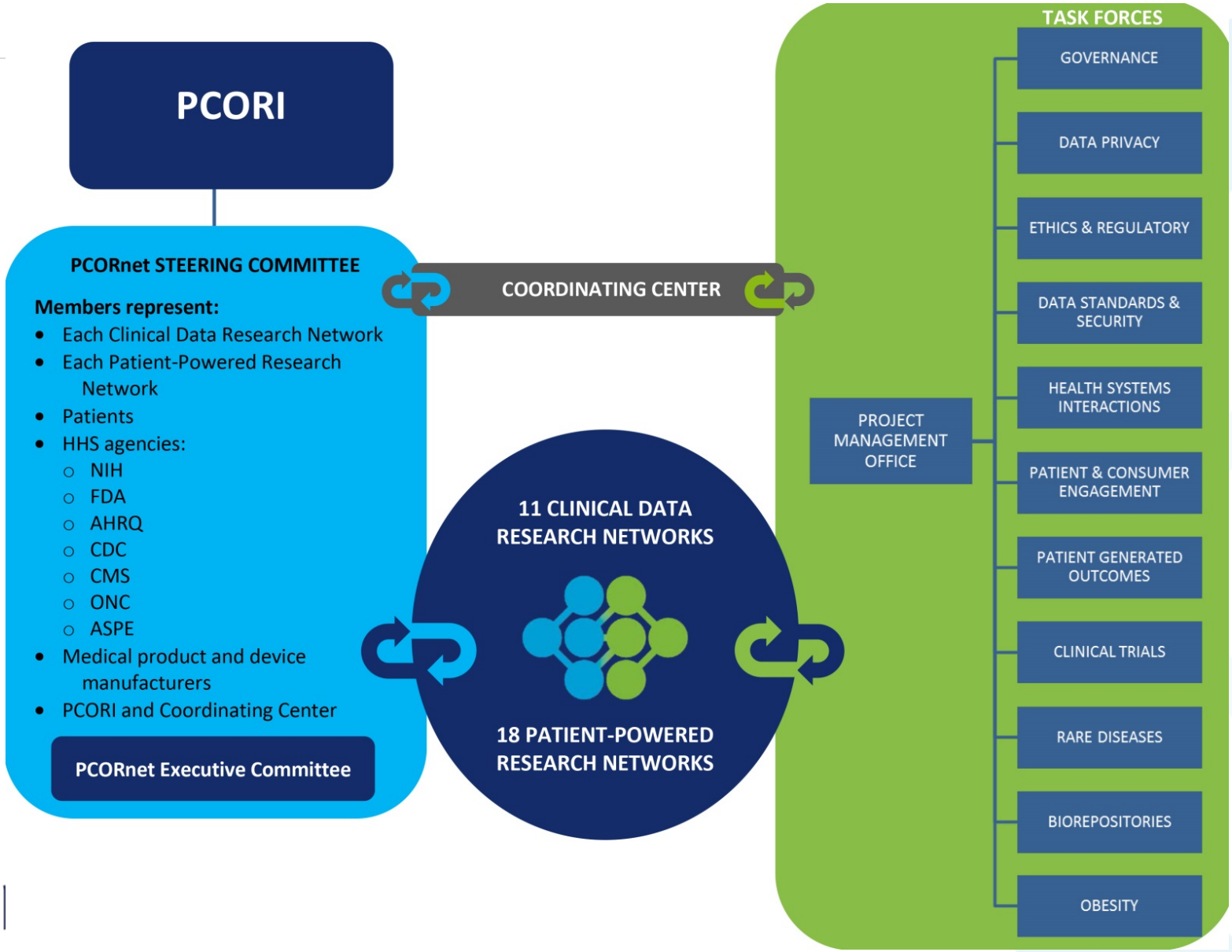
PCORnet organizational structure



29 CDRN and PPRN awards were approved on December 17th by PCORI's Board of Governors

This map depicts the number of PCORI funded Patient-Powered or Clinical Data Research Networks that have coverage in each state.

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CDRN Partners

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The National Patient-Centered Clinical Research Network

Goals for Each Clinical Data Research Network (CDRN)

- Create a research-ready dataset of at least 1 million patients that is:
  - **Secure** and does not identify individual patients
  - **Comprehensive,** using data from EHRs to describe patients' care experience over time and in different care settings
- Involve patients, clinicians, and health system leaders in all aspects of creating and running the network
- Develop the ability to run a clinical trial in the participating systems that fits seamlessly into healthcare operations
- Identify at least 3 cohorts of patients who have a condition in common, and who can be characterized and surveyed

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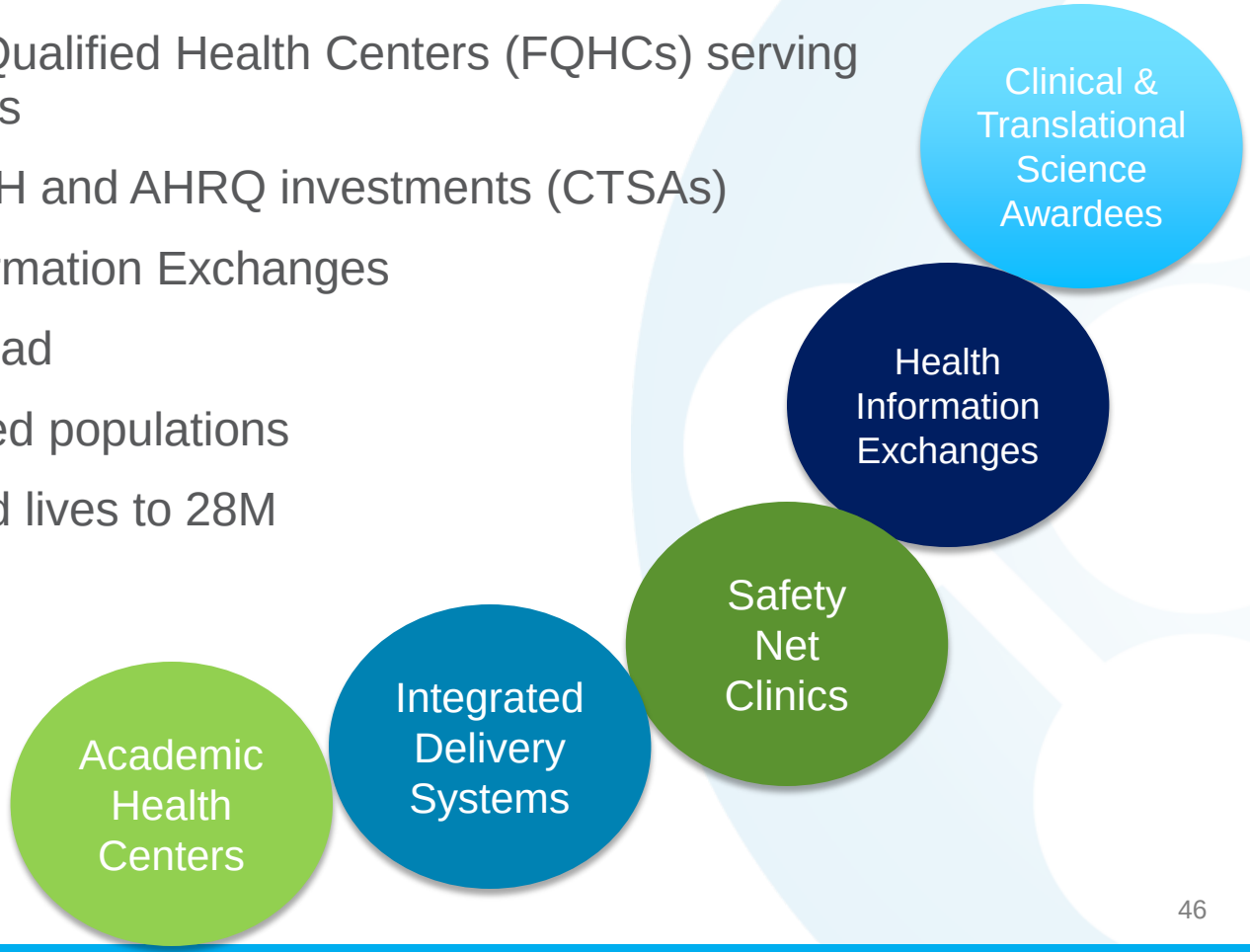
CDRN highlights

- Networks of academic health centers, hospitals & clinical practices
- Networks of non-profit integrated health systems
- Networks of Federally Qualified Health Centers (FQHCs) serving low-income communities
- Networks leveraging NIH and AHRQ investments (CTSAs)
- Inclusion of Health Information Exchanges
- Wide geographical spread
- Inclusion of under-served populations
- Range from 1M covered lives to 28M



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PPRN Partners

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The National Patient-Centered Clinical Research Network

Goals for each Patient-Powered Research Network (PPRN)

- Establish an activated patient population with a condition of interest (Size >50 patients for rare diseases; >50,000 for common conditions)
- Collect patient-reported data for ≥80% of patients in the network
- Involve patients in network governance
- Create standardized database suitable for sharing with other network members that can be used to respond to “queries” (ideas for possible research studies)

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PPRN highlights

- Participating organizations and leadership teams include patients, advocacy groups, clinicians, academic centers, practice-based research networks
- Strong understanding of patient engagement
- Significant range of conditions and diseases
- Variety in populations represented (including pediatrics, under-served populations)
- 50% are focused on rare diseases
- Varying capabilities with respect to developing research data
- Several PPRNs have capacity to work with biospecimens

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ALD Connect

Engagement

- A collaboration between patients, patient advocacy groups, and academic centers.

Potential Impact

- Improve care for and ultimately eradicate the debilitating single-gene disorder, X-linked Adrenoleukodystrophy (ALD).

Objectives

- Create a social network platform that allows for dynamic engagement of the patient community and that will allow for data comparison and validation, patient feedback on research directions, and more rapid trial development.

Through direct participation in decisions on research and drug development, patients will influence research priorities and directions. The ALD Connect collaborative network will introduce a novel all-inclusive model to improve care and drug discovery for well-defined single-gene disorders.

Florian Eichler, MD
ALD Connect, Inc

CER Methods and Infrastructure, awarded December 2013

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Community-Engaged Network for All (CENA)

Engagement

- Use of participant-led governance models, bringing leaders and affected individuals from each condition community together to oversee CENA.

Potential Impact

- Shift research culture from one where academic researchers reach out to participants, to one where participants lead.

Objectives

- The Platform for Engaging Everyone Responsibly (PEER) will allow for extremely cost-effective data capture from participants in a manner that ensures granular privacy permissions management.

A network of 10 Disease Advocacy Organizations (DAOs): Alström Syndrome International, Dyskeratosis Congenita Outreach, Inflammatory Breast Cancer Research Foundation, Hepatitis Foundation International, Joubert Syndrome Foundation, KS&A, MLD Foundation, National Gaucher Foundation, National Psoriasis Foundation, and PXE International.

Sharon Terry, MA
Genetic Alliance, Inc

CER Methods and Infrastructure awarded December 2013

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DuchenneConnect Patient-Report Registry Infrastructure Project

Engagement

- Guided by a multidisciplinary advisory committee that includes parents and individuals with Duchenne/Becker muscular dystrophy (DBMD).

Potential Impact

- Provide clinically relevant results that are of importance to the DBMD patient community.

Objectives

- Collect robust, longitudinal patient-reported data for use by industry, clinicians, and academic researchers.

We must balance obtaining sufficient and robust information with the monitoring burden and providing participation benefits back to registrants. We must explore novel data collection approaches, including EHR integration to reduce registrant burden, allowing evaluation of the accuracy of specific patient-report outcomes, and improving our capacity to answer questions about natural history and care.

Holly Peay, MS
Parent Project Muscular Dystrophy

CER Methods and Infrastructure, awarded December 2013

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NephCure Kidney Network for Patients with Nephrotic Syndrome

Engagement

- A network governance structure that includes substantial patient representation to ensure patient involvement in policy development and key decision making.

Potential Impact

- Improve diagnostic, prognostic, and therapeutic advances for primary Nephrotic Syndrome (NS).

Objectives

- Transform a static repository of limited cross-sectional data to a rich clinical and patient-reported outcomes (PRO) database, with patients as active participants to facilitate efficient and accurate CER.

The establishment of a research network with readily available clinical and patient-reported data, an organizational structure that includes patients in the governance process, and direct partnership with patients who are seeking opportunities to be a part of the solution for better health will facilitate much-needed advances for patients with this rare and devastating condition.

Bruce M. Robinson, MD, MS
Arbor Research Collaborative for Health

CER Methods and Infrastructure, awarded December 2013

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Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium

Engagement

- Shared governance model of patients, family members, and other stakeholders including healthcare providers, advocacy groups, a clinical research network, and a quality improvement learning network.

Potential Impact

- Improve outcomes for children with the most prevalent pediatric rheumatic diseases.

Objectives

- Coordinate and standardize data collection and sharing across the consortium, extend existing online platforms for (PROs) and direct data transfer from electronic health record (EHR) to PARTNERS database.

PARTNERS will drive forward research based on patient-centered scientific priorities and integrate patient input into all aspects of research, from study design to analyses, creating a patient-centered learning health system.

Laura Schanberg, MD
Duke University

CER Methods and Infrastructure, awarded December 2013

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Phelan-McDermid Syndrome Data Network

Engagement

- Founded by parents, the registry is driven by parents, governed by parents, and will be transformed by parents.

Potential Impact

- Provide family support and to accelerate research for individuals with PMS.

Objectives

- Build a dedicated data network to enable scientists to have access to all available knowledge from PMS patients. Multiple data feeds will be established to extract and link data securely, while maintaining privacy and ethical safeguards.

PMSF has pioneered the concept of the patient-driven registry within a population of patients with a rare condition, through the perseverance of devoted parents. This registry provides a solid foundation upon which to build a network that can create new information in the form of meaningful data for researchers.

Megan O'Boyle, BA
Phelan-McDermid Syndrome Foundation

CER Methods and Infrastructure, awarded December 2013

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PI Patient Research Connection: PI-CONNECT

Engagement

- Leverage a strong bond with the Primary Immunodeficiency (PI) community, including patients, clinicians, and researchers, based on trust, reliability, and understanding.

Potential Impact

- Improving the diagnosis, treatment, and quality of life of persons with PI.

Objectives

- Meld two data sets (a curated, data-validated, longitudinal registry of patient data and a data set produced to give patients a unified home for their medical information) to maximize the breadth of data and to promote improvements in patient care.

PI CONNECT will create a venue for researchers and patients to communicate about proposed research involving the network data, giving patients a voice in research, as well as giving researchers better access to the PI community.

Kathleen Sullivan, MD, PhD
Immune Deficiency Foundation

CER Methods and Infrastructure, awarded December 2013

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Rare Epilepsy Network (REN)

Engagement

- Created by and for patients to provide patients and their families an opportunity to participate in research.

Potential Impact

- Improve lives and quality of care for people with catastrophic rare epilepsies.

Objectives

- Policy creation, development of standards, outreach and member engagement to create a robust patient-centered research enterprise for rare epilepsies.

EF has a strong commitment to supporting the best research possible to both improve care and to promote cures of epilepsy for patients.

Janice M. Buelow, PhD, RN
Epilepsy Foundation

CER Methods and Infrastructure, awarded December 2013

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Vasculitis Patient Powered Research Network

Engagement

- Expand the role of patients such that they are fully involved in direct network governance.

Potential Impact

- Conduct high-quality clinical research in vasculitis aimed at addressing key scientific and clinical issues considered of high priority to both patients and physicians.

Objectives

- Increase membership and patient representation, expand data access and availability, and address disease-specific outcomes.

The V-PPRN will be a vibrant, flexible, sustainable patient community ready and committed to participate in clinical research through sharing of electronic medical records to address important issues facing patients and other stakeholders.

Peter Merkel, MD, MPH
University of Pennsylvania

CER Methods and Infrastructure, awarded December 2013

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The PCORnet opportunity: making a real difference for patients and their families

Until now, we have been unable to answer many of the most important questions affecting health and healthcare

By combining the knowledge and insights of patients, caregivers, and researchers in a revolutionary network with carefully controlled access to rich sources of health data, we will be able to respond to patients' priorities and speed the creation of new knowledge to guide treatment on a national scale.

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Lunch

12:00 – 1:00 p.m. EST

Patient-Centered Outcomes Research Institute

Open Discussions

Moderated by:

Bryan Luce, PhD, MBA

Chief Science Officer, PCORI

Patient-Centered Outcomes Research Institute

Discussions Part 1: Moderated by Bryan Luce

- Topic 1: Provide input to PCORI on research needs of the rare diseases community and on specific issues and concerns in conducting research on rare diseases
- Topic 2: Advise other PCORI committees and panels to ensure the unique considerations of rare disease are addressed

Discussions Part 2: Moderated by Jean Slutsky

- Topic 1: Provide ongoing feedback and advice on evaluating and disseminating PCORI's research portfolio on rare diseases
- Topic 2: Consider study findings and advise on targets and strategies for PCORI dissemination efforts
- Topic 3: Identify opportunities for collaboration with existing international, federal, public and private entities doing similar work in the rare disease space

Break

4:00 – 4:15 p.m. EST

Patient-Centered Outcomes Research Institute

Organizational Issues: Meeting Frequency, Scheduling, Leadership, and Staff Support

Kara Odom Walker, MD, MPH, MSHS
Deputy Chief Science Officer, PCORI

Patient-Centered Outcomes Research Institute

Topics

- Meeting frequency
- Scheduling: Next two face-to-face meetings
  - HOLD: September 29 – October 2, 2014 (Fall 2014 meeting)
  - HOLD: January 12 – 15, 2015 (Winter 2015 meeting)
- Leadership: Please submit nomination (including self-nominations) to RDAP@pcori.org. PCORI staff will then select a chair and co-chair and will announce the new leadership to all panel members.
- Staff support

Recap and Next Steps

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI

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Adjourn

Thank you for your participation!