



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

## Advisory Panel on Rare Disease Meeting Summary

### Overview

On April 26, 2017, the PCORI Advisory Panel on Rare Disease (RDAP) held its seventh meeting in Washington, DC.

RDAP's 15 members include patients, caregivers, representatives of patient advocacy organizations and industry, clinicians, payers, and researchers. The meeting was open to the public via webinar, and meeting PowerPoint slides were posted to the PCORI website in advance.

RDAP received updates on the rare disease research funded by PCORI's Eugene Washington Engagement Award Program, a webinar on PCORI funding opportunities and resources for rare disease organizations, and updates to PCORI's rare disease website. The RDAP also discussed the implications of making revisions to PCORI's merit review criteria to specify unique considerations when reviewing rare disease research applications. The RDAP learned about the status of the report, *An Overview of the Impact of Rare Disease Characteristics on Research Methodology*, and discussed the need for a core outcomes set for rare diseases and how to develop this resource. RDAP members responded to presentations on rare disease activities at the National Center for Advancing Translational Science at the National Institutes of Health and at PCORnet, the National Patient-Centered Clinical Research Network, by recommending collaborations between these programs. A final discussion addressed potential future activities for the panel.

### Related Information

- [About this Advisory Panel](#)
- [Meeting Details and Materials](#)
- [Advisory Panel on Rare Disease October 27, 2016, Meeting](#)
- [PCORI's Rare Disease Landing Page](#)
- [Rare Disease Research Guide for Merit Reviewers](#)
- [Rare Diseases Clinical Research Network](#)
- [PCORnet, the National Patient-Centered Clinical Research Network](#)

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed healthcare decisions.

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## Rare Disease Engagement and Research Webinar and Web Page Updates

Lia Hotchkiss, Director of PCORI's [Eugene Washington Engagement Award Program](#), reminded the RDAP that this program supports projects that build communities able to participate in patient-centered outcomes research (PCOR) and comparative clinical effectiveness research (CER), and that serve as channels for disseminating study results. The program funds engagement award projects to build the knowledge base for participation in PCOR/CER and meetings/conferences that facilitate expansion of PCOR/CER. Since PCORI's Engagement Award Program started in 2014, it has funded over 200 projects and conferences for a total budget of \$39 million. To date, the program has funded 24 projects focused on rare diseases, representing approximately 10% of the program budget.

Jacqueline Gannon, National Urban Fellow at PCORI, described an April 20, 2017, [webinar](#) on PCORI funding opportunities and resources for rare disease organizations. According to a participant survey of the 89 attendees, the webinar provided useful information on PCOR, engagement in research, and PCORI's funding streams. PCORI's [rare disease landing page](#) now features details on all of PCORI's funded rare disease projects, rare disease-specific resources for applicants, past webinars and town halls, and PCORI media (including blogs and videos).

RDAP members offered the following recommendations:

- Identify the stakeholder affiliations of individuals who attended the webinar
- Use the content from the webinar's Q&A session to develop a set of frequently asked questions for the rare disease landing page (and consult RDAP about additional questions to include)
- Make the rare disease landing page easier to find, through searches for "rare disease" in the PCORI website's search box or when searching for specific rare diseases

## Guidance for Merit Reviewers

Dr. Danielle Whicher, Program Officer for Clinical Effectiveness and Decision Science at PCORI, asked RDAP members to review the draft [Rare Disease Research Guide for Merit Reviewers](#), which lists topics the RDAP members previously compiled for PCORI merit reviewers to consider when reviewing research applications that deal with rare diseases. PCORI staff discussed the risks and benefits of incorporating this information into the [merit review criteria document](#) for reviewers of broad, targeted, and pragmatic clinical studies.

The RDAP recommended that PCORI not make the proposed additions to the PCORI merit review criteria. Instead, they recommended that PCORI:

- Ensure that PCORI staff indicate to merit reviewers which applications focus on rare diseases
- Determine proportions of rare disease research applications to PCORI that are rejected and why, to determine if any of the reasons are specific to rare disease applications
- Train merit reviewers on the unique challenges of rare disease studies
- In the merit review panels, include statisticians who are familiar with the statistical techniques that are appropriate for rare disease studies with small samples

## Rare Disease Methodology Paper Update

Dr. Whicher gave an update on a draft report, *An Overview of the Impact of Rare Disease Characteristics on Research Methodology*, prepared by a small group of RDAP members under Dr. Naomi Aronson's leadership. The purpose of the report was to raise awareness of methodological and analytic approaches that are relevant to rare disease research. The RDAP and the PCORI [Methodology Committee](#) have now reviewed and provided feedback on the draft report, and the Methodology Committee will consider a revised version at its meeting on May 1, 2017. Once the committee approves the document, it will be posted on the PCORI website, and a peer-reviewed paper will be developed.

## Core Outcome Sets for Rare Diseases

Dr. Whicher explained that at the RDAP's October 2016 meeting, the panel had recommended that PCORI explore past examples and possible future directions for the development of a core set of outcomes for rare diseases. She invited RDAP members to discuss the aims of this initiative.

The RDAP expressed interest in developing patient-centered core outcomes for rare diseases, with a particular focus on rare diseases affecting pediatric populations. The discussion reflected that a core outcomes set would help make rare disease research more patient centered, make it easier to combine the results of different rare disease studies, and measure patient-reported outcomes during every clinical encounter to improve quality of care and outcomes. The RDAP agreed that it was important to focus on developing core outcomes sets for pediatric rare diseases because most rare diseases affect children. The panel also recommended that this effort build on the National Institutes of Health (NIH) [Patient Reported Outcomes Measurement Information System \(PROMIS\)](#).

The RDAP offered the following additional recommendations:

- Ensure that the set includes core outcomes that are specific to children and encompasses factors unique to rare diseases that might not be included in PROMIS (e.g., function in school, social adaptation, cognitive development, speech and language skill development, etc.)
- Focus on core outcomes that can be collected by the patient or caregiver with low burden and do not require clinician input
- Include outcomes that are important to patients and relevant to all children with rare diseases, regardless of age, such as activities of daily living, developmental and occupational therapy milestones, quality of life, and caregiver burden
- Examine existing core outcome sets for children that could capture the social, functional, and developmental outcomes related to quality of life that are critical to children
  - Then bring in the rare disease perspective for identifying the unique elements to capture for the domains of function, participation, and well-being
- Identify core outcomes from the PCORI portfolio of funded studies in rare diseases
- Develop some optional disease-specific outcomes

## National Center for Advancing Translational Science (NCATS) Rare Disease Activities

Dr. Anne Pariser, Deputy Director of the Office of Rare Disease Research (ORDR), described several rare disease initiatives at NCATS, one of the 27 NIH institutes and centers. NIH spends approximately \$3 billion a year on rare disease research, and 90% of this funding goes to extramural programs. The mission of the ORDR is to facilitate, support, and accelerate the translation of rare disease science to benefit patients. Major initiatives related to rare diseases at ORDR and NCATS are:

- Global Rare Diseases Patient Registry Program 2
- [Genetic and Rare Diseases Information Center](#)
- Funding for scientific conferences
- Toolkit for Patient-Focused Drug Development (to be launched on September 8, 2017)

Dr. Rashmi Gopal-Srivastava, Director of the Extramural Research Program at ORDR, described the [Rare Diseases Clinical Research Network \(RDCRN\)](#), which is led by NCATS in collaboration with 10 other NIH institutes and centers. The program's goals are to make meaningful large-scale clinical studies possible, collaborate with patient advocacy groups as research partners, train new investigators, support pilot projects, and provide online education and research resources.

The program currently supports five consortia that conduct longitudinal studies (which must include natural history studies and can also include clinical trials) on at least three related rare diseases. Collectively, the RDCRN is studying 200 rare diseases at 418 clinical sites in the United States and 24 other countries.

## Leveraging PCORnet

Dr. Maryan Zirkle, Program Officer for Research Infrastructure at PCORI, explained that [PCORnet, the National Patient-Centered Clinical Research Network](#), is a network of 20 patient-powered research networks (PPRNs) and 13 clinical data research networks (CDRNs) that represents approximately 110 million patients. Each CDRN must study a common disease cohort and a rare disease cohort. Dr. Claudia Grossmann, Program Officer for Research Infrastructure, reported that PCORnet's 20 PPRNs include nine networks that focus on rare diseases with more than 29,000 patients who have consented to participate in research to date.

The PCORnet [Front Door](#) enables PCORnet researchers and other investigators, patient groups, health-care organizations, clinicians, government and industry scientists, and sponsors to collaborate on important patient-centered clinical research studies through PCORnet. PCORnet is a distributed research network, which means that all data are held locally. To use PCORnet resources, a researcher must send a question to the PCORnet coordinating center through the Front Door. PCORnet can be used for pre-research feasibility queries and matchmaking, observational studies, and interventional studies.

The RDAP asked which rare diseases are studied in both the RDCRN and PCORnet, which might be useful for developing a core outcomes set. It might be possible to combine cohorts with the same disease from both programs. RDAP also suggested that NCATS and PCORI co-fund some rare disease studies.

## Other Areas of Interest

Dr. Parag Aggarwal, Senior Program Officer for the Healthcare Delivery and Disparities Research Program at PCORI, described a draft framework that PCORI is developing for RDAP that includes the committee's vision, current topics, and potential future activities. He asked RDAP members to describe their interest in the activities listed in the framework, as well as other activities.

The RDAP suggested a navigator program for applicants proposing rare disease studies to PCORI, to be developed in consultation with PCORI's [Advisory Panel on Clinical Trials](#) and [Methodology Committee](#). This program could identify the barriers to successful applications and help applicants overcome these barriers, and provide information that could include education on how to obtain institutional review board approval, assistance in developing effective partnerships, identification of other funders for projects that do not match PCORI's funding priorities, and statistical consultation to ensure that proposed studies have adequate statistical power..

The RDAP considered ways to bring together the issues discussed at this meeting, including PCORnet and NCATS initiatives and the creation of a core outcomes set for rare diseases. For example, the CDRNs have already identified rare diseases of interest to them, and NCATS might be interested in pursuing some of these diseases. These joint PCORnet and NCATS studies could include core outcomes of interest to patients. Furthermore, some common data elements for rare diseases might be available in the PCORnet and NCATS databases to be aggregated. Alternatively, PCORI staff could convene an expert workgroup to develop core outcomes and then work with an organization to develop these measures. This workgroup could lead to the creation of a plan that could be used as the basis for a request for proposals to develop the core outcomes.

The RDAP suggested that PCORI survey RDAP members about topics of greatest interest. They also agreed that PCORI should reanalyze rare disease applications and letters of intent that are not successful to identify barriers and use this information to provide guidance to merit reviewers and applicants.

## Closing

Vincent Del Gaizo, Co-chair of the RDAP, acknowledged the contributions of RDAP members whose terms were ending: Dr. Marilyn Bull, Dr. Uday Deshmukh, Dr. Sindy Escobar-Alvarez, Dr. Kate Lorig, and Dr. Mark Skinner. Each member received a plaque recognizing his or her service on the panel.

Dr. Matt Cheung, RDAP Chair, summarized the meeting by noting that it had addressed:

- PCORI's engagement awards and how they could benefit the rare disease community
- The PCORI rare disease website
- A process for ensuring that merit reviewers understand the challenges of rare disease research and potential RDAP activities in this area
- Development of a core outcomes set for rare diseases
- Rare disease research projects in PCORnet and at NCATS and the possibility of collaborations among these programs