Advisory Panel on Rare Disease Advisory Panel

June 2018

Overview

The Patient-Centered Outcomes Research Institute (PCORI) Advisory Panel on Rare Disease (RDAP) held its 11th meeting on June 6, 2018, in Washington, DC. (The meeting was originally scheduled for March 21, 2018 but was canceled due to inclement weather.)

RDAP's 13 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 materials were posted to the PCORI website in advance.

PCORI staff outlined current dissemination activities and implementation efforts and broad opportunities around the rare diseases portfolio. The RDAP offered recommendations for reaching more stakeholders. Next, Dr. Benjamin M. Greenberg described his study's novel approaches to addressing challenges in conducting rare disease research, which relied heavily on collaboration with a patient organization and implementing unique tools for capturing participant outcomes data. Pam Gavin then gave an overview about the National Organization for Rare Diseases and discussed potential opportunities for collaboration with PCORI. Following, Dr. Peter Margolis outlined a model Learning Healthcare Systems network for gathering patient and clinician information in a way that promotes best practices and enables the affected community to develop tools and materials that can assist patients and spur changes in treatment.

Following an update on RDAP accomplishments, members discussed future agenda items. The panel concluded with acknowledging retiring members and thanking them for their service.

Related Information

- About this Advisory Panel
- Meeting Details and Materials
- Rare Diseases Advisory Panel September 2017 Meeting Summary
- PCORI: Putting Evidence to Work
- National Organization for Rare Disorders
- PCORI: Rare Diseases

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

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Dissemination and Implementation: Updates, Challenges, and Opportunities

Dr. Joanna Siegel, PCORI Director of Dissemination and Implementation, discussed with the panel the difference between dissemination, which is the process of identifying target audiences and tailoring communication to them, from implementation, which is the process of integrating evidence into practice. Once PCORI research results are finalized, PCORI, in collaboration with the Translation Center, publishes the findings in two formats, one designed for professionals, the other for the lay audience. Siegel emphasized that the materials aimed at professionals focus on the impact and application of the findings in clinical practice. Dr. Parag Aggarwal added that PCORI's Open Science Initiative aims to find ways researchers can enter their data into a publicly accessible repository to enhance data sharing.

PCORI supports implementation through a variety of different awards. One award encourages PCORI-funded investigators to continue working with their partners on the ground to implement their findings while another focuses specifically on shared decision-making. A third award was recently approved to attract more expertise in implementation science. To bolster dissemination, PCORI also offers engagement awards to those working closely with stakeholders in the field and for building capacity for dissemination. PCORI also publishes evidence updates and offers continuing medical education programs.

In response to questions, Siegel clarified that PCORI-funded research awardees must include a feasible dissemination and implementation plan in their applications, but PCORI does not fund the plan as part of the initial award because the research findings must be reviewed to ensure quality. As researchers near the end of their projects, PCORI staff work directly with them to put the plan into action. PCORI relies on its ambassadors to further disseminate information. More information and details are available on PCORI's web page, Putting Evidence to Work.

The Panel provided the following suggestions on dissemination and implementation:

- Ask ambassadors to review PCORI publications (e.g., the abstracts).
- Encourage rare disease organizations to post relevant findings or link to them on the PCORI website.
- Consider how findings from one study population may translate to other, perhaps narrower or rare, populations and target them for dissemination, if appropriate.
- Add an overview of the PCORI dissemination and implementation approach to the informational slide set used by RDAP and others to educate people about PCORI.
- Develop a fact sheet on dissemination and implementation issues unique to the rare diseases community (which can also promote outreach to international rare disease organizations).

RDAP suggested that at a future meeting, the panel would like to review a funded dissemination award for rare disease research to assess whether the requirements for dissemination and implementation plans consider issues unique to the rare diseases community.

PCORI Case Study: Collaborative Assessment of Pediatric Transverse Myelitis

Dr. Benjamin Morris Greenberg of the University of Texas Southwestern Medical Center in Dallas, TX, described the novel approaches used in his PCORI funded rare disease study to recruit more participants and yield more meaningful data than previous studies of the condition. Dr. Greenberg noted the following critical aspects of the intervention and the study approaches:

- Participants could take part in person or be part of a virtual cohort. Much of the same data were captured from both cohorts, including quality-of-life issues and patient-reported outcomes. The setup allowed investigators to compare clinician-derived data with patient-reported information and thus assess the validity of patient-reported outcomes against the standard outcomes that clinicians gather.
- The study funded an ambassador—a parent of a child with transverse myelitis—who worked at the Transverse Myelitis Association (TMA) to identify study candidates through social media and outreach and then approach them about participation. The ambassador's personal experience with the disease and empathy were instrumental in recruitment. The ambassador began as a TMA volunteer, then became a part-time member of the TMA staff with funding from the study protocol.
- The TMA will host a publicly accessible and searchable database of results so that researchers and clinicians can uncover what worked for whom. The database was developed by Traitwise and will be maintained by the TMA beyond the study protocol. The database will be open to data input from other investigators. Guardrails are in place to ensure that information is not identifiable and to protect against misuse of the data.
- The TMA's database has been approved by an institutional review board. At present, users can contact the investigators to discuss the results. The investigators have requested PCORI funding to test methods for helping users with data interpretation as part of dissemination. The study ambassador will help disseminate the study results and will be part of the team that maintains the TMA database.

Dr. Greenberg emphasized that true collaboration with stakeholder partners is especially important for rare disease research, as rare disease organizations are uniquely intertwined with patients and families. He urged PCORI to develop criteria and models for such partnerships, including funding mechanisms that can support small stakeholder organizations. He also called for a push for more research that can validate the utility of patient-reported outcomes, more requirements for data sharing, and sustainable assets, such as databases, that outlive their study protocols.

Finally, Dr. Greenberg suggested for RDAP to help PCORI directly partner with patient advocacy organizations for study recruitment. Furthermore, RDAP could advise PCORI on creating common tools for data sharing and common approaches to sustainable assets.

Panel members noted that organizations like Google and Facebook may be willing to promote rare disease research protocols and registries at no cost, as a public health service.

Update on the National Organization for Rare Disorders (NORD)

Pam Gavin, NORD's chief strategy officer, gave an overview of the organization, stating NORD represents all known rare disorders that occur in the United States and has no industry involvement. NORD works with patient organizations and advocates, medical students, and biopharmaceutical companies, among others. In addition to supporting research, NORD is committed to ensuring that research translates to treatment, that patients have access to treatment, and that treatments work as intended.

The U.S. Food and Drug Administration (FDA) indicated that it is difficult to assess the burden and natural progress of disease without the extensive supporting data usually provided by drug sponsors. In response, NORD established a registry, IAMRARE, to facilitate natural history studies. NORD worked with the National Institutes of Health and the rare diseases group within FDA's Center for Drug Evaluation and Research to make IAMRARE available as a data resource to researchers with limited financial or staff resources. NORD has projects underway allowing partners to use the IAMRARE registry data; one for-profit partner calculated that using the registry decreased their drug development time by one year. At present, researchers who want access to the data must work directly with NORD. Currently, data-sharing protocols and templates are in place for an effort to create a portal to let users query the database to identify populations of interest. As part of the informed consent process, individuals who provide information to IAMRARE indicate their willingness to be contacted about clinical trial participation.

NORD and FDA launched a series of listening sessions to bring patient voices into the research process and educate patients and families about the FDA and drug development. NORD is archiving the listening sessions, which may eventually inform reimbursement discussions. Since 1989, NORD has awarded 150 grants totaling $7 million for rare disease research, often as seed funding. Awards have resulted in more than 100 peer-reviewed publications in major journals and two FDA-approved treatments.

The Panel made the following suggestions for PCORI and NORD:

- There is potential for NORD and PCORI to collaborate around the FDA listening sessions, the IAMRARE registry, development of training and best practice tools for patient-centered outcomes research in rare diseases, and NORD's RareInsights online platform for education and outreach.
- In addition to medical and pharmacy students, NORD should consider expanding educational outreach to other health care professionals, such as nurses, physical and occupational therapists, nutritionists, and dietitians. (NORD is already working with genetic counselors and is discussing a partnership to offer internships to bioinformatics students.)
- NORD may wish to determine how much federal funding has gone toward rare disease research, as the findings may demonstrate NORD's impact.
- NORD's Rare Insights platform may be a useful mechanism for disseminating PCORI findings.

Healthier Together: Networks of Patients, Clinicians, and Researchers to Transform Chronic Illness Care

Dr. Peter A. Margolis, co-director of the James M. Anderson Center for Health Systems Excellence, described the learning healthcare system network ImproveCareNow. ImproveCareNow is a network that combines learning, communication, and practice and has resulted in a continuous cycle of care improvement. This network harnesses the collective intelligence of patients and their clinicians, operating on the same premise as social media that, given effective tools, individuals will organize around shared purposes and cooperate to share resources.

ImproveCareNow, a network for pediatric Crohn's disease, was established in 2007. The network model captures information from electronic health records and registries of patient-reported outcomes, then feeds those data back to clinicians. Outcomes data are compared against specified targets, triggering a continuous quality improvement cycle of directed research and feedback. The public-facing component of the model provides a user-designed platform for sharing information. The network has been a success—as more sites joined the network and began sharing clinician and patient information and experiences, the percentage of pediatric Crohn's patients in remission has increased steadily even though no new medications for the condition have been developed.

Most patients with rare diseases lack trust in the system and do not feel empowered. ImproveCareNow's relentless focus on outcomes acts as a fulcrum for sharing data, increasing transparency, and continuously drawing attention back to the issues that matter most to patients. With this learning network, clinicians can show patients real-world data gathered from other patients.

A similar learning network has been modeled off of ImproveCareNow for the Cystic Fibrosis Foundation's registry and quality improvement approach. This network was designed to incorporate more transparency and feedback, with the ultimate goal to create a community where a few people are creating tools and materials, and many nationwide are learning from them. This community "self-curates" to ensure that materials are reasonable, and medical experts screen the materials to correct misinformation.

The Panel raised concerns that those with limited access to technology or low digital literacy might not benefit from the tech-heavy approach of the model.

Update: PCORI Rare Disease Topic Page and Resources

Bill Silberg, PCORI's director of communications, and Santosh Rao, web editorial specialist, presented an update to PCORI's Rare Diseases web page based on the Panel's feedback during the Fall 2017 in-person meeting. Users can navigate to the full portfolio of projects on a given topic, filter the results to find specific interests, and link to the results of completed projects.

PCORI's website includes links to organizations like NORD, especially if those organizations have published data of interest. PCORI regularly reaches out to stakeholder groups and relies on them to further disseminate results. PCORI works with stakeholder groups to determine what kinds of information they need.

PCORI is seeking individuals willing to relay their personal stories (as patients, caregivers, advocates, or clinicians) related to rare diseases. PCORI would also like to support individuals in sharing their stories with their local media outlets. In some cases, PCORI may be funding projects in a local market that can be highlighted along with personal narratives.

The Panel recommended RDAP members give feedback on future PCORI web pages related to rare disease, and work with the Communications Department to increase dissemination and implementation for rare disease.

RDAP Planning

RDAP Co-Chair Dr. Matt Cheung described activities accomplished by the RDAP and some items yet to be completed. He presented a list of potential topics and speakers for future agendas, compiled from members' comments and previous discussions.

The Panel expressed interest in pursuing the following topics for future discussion:

- Assisting patient advocacy organizations with developing research proposals for PCORI, e.g., with tailored tools or advice for the rare diseases community
- Patient partners' experience with research, particularly barriers to success
- Understanding the importance of studying the natural history of disease and what is important to caregivers (although this was deemed to be beyond PCORI's scope, which is limited to comparative effectiveness research)

Immediate options for assisting the rare disease community with applying for PCORI funding include:

- educating the community about using the PCORI help desk,
- disseminating contact information for the PCORI rare diseases staff, and
- publicizing the archived webinar, "PCORI Opportunities for Funding and Resources for Rare Disease Organizations."

RDAP will survey members about topics to address in future panel meetings.

The Panel expressed the desire to be able to extend panel term limits, as they feel the 3-year appointment may be too brief for those who serve to make progress towards the Panel's goals. However, this is a decision that must be made by PCORI leadership.

Closing and Next Steps

Panel member Cindy Luxhoj will take Vincent Del Gaizo's place as co-chair beginning at the next meeting. Dr. Cheung thanked the retiring RDAP members for their service:

- Vincent Del Gaizo
- Patricia Furlong
- Lisa Heral
- Dr. Yaffa Rubenstein
- James Wu