National Organization for Rare Disorders (NORD)
Rare Diseases & Orphan Products
Breakthrough Summit
Arlington, VA
Track VI: Patient-Centered Outcomes Research
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Patient-Centered Outcomes Research: What it Means to the Rare Disease Community
Presenters

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Learning Objectives

At the end of this session, participants will be able to:

• Recognize the various definitions of PCOR and define PCOR with respect to the rare-disease community

• Differentiate PCOR from traditional healthcare research (e.g., NIH-funded research, roadmap to discovery)

• Describe the hallmark characteristics of PCOR and types of study designs and methods used

• Cite examples of PCOR in rare disease arena and work being done by rare disease organizations
Session Overview

1. PCOR and Rare Diseases: A NORD Perspective
   Pamela Gavin, National Organization for Rare Disorders

2. Patient-Centered Outcomes Research (PCOR) 101
   Eleanor Perfetto, University of Maryland School of Pharmacy

3. Case Example
   Christine Brown, National PKU Alliance

4. Questions and Discussion
PCOR and Rare Diseases: The NORD Perspective

Rare-disease patient advocacy groups participate in research studies because of their interest in biomedicine and their experience in biomedical research

True  False
Rare-disease patient advocacy groups participate in research studies because of their interest in biomedicine and their experience in biomedical research.

True
PCOR and Rare Diseases: The NORD Perspective

• Rare-disease patient advocacy groups are driven to participate in research because:
  • The disease has affected them or someone they know
  • They have an urgent need to advance their cause and are driven to participate in research
  • Most groups are ready and willing!
PCOR and Rare Diseases: The NORD Perspective

- The relationship between rare-disease patients’ perspectives and treatment outcomes have not been well studied.
- Researchers need to understand:
  - Outcomes desired by rare-disease patients, family members, and caregivers
  - Where and how treatments are provided
  - Unique challenges the rare-disease community faces
- Rare-disease patient advocacy groups should be trained in PCOR to:
  - Better advise researchers on how to make research more meaningful to rare-disease patients
  - Directly develop, shape, and fuel research (e.g., act as PIs)
Terms/Definitions

**Efficacy** trials – “determine whether an intervention produces the expected result under *ideal* circumstances”

*Can it work?*

**Effectiveness** trials – “degree of beneficial effect under ‘real-world’ clinical settings”

*Does it work in “real-world” populations?*

Terms/Definitions

Comparative effectiveness (IOM 2009)

“...is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.” The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.”

Efficacy versus Effectiveness versus *Comparative* Effectiveness

What if there is no “Intervention B?”
Comparative Effectiveness for the Rare Disease Community

“Real World” Populations

Effectiveness

Intervention A
Placebo

Comparative Effectiveness

Intervention A
Intervention B

OR

Standard of care

What if there is no “Intervention B?”

“Researchers should make explicit what the comparators are and how they were selected, focusing on clearly describing how the chosen comparator(s) define the causal question, reduce the potential for biases, and allow direct comparisons. Generally, non-use (or no specific treatment) comparator groups should be avoided unless no specific treatment is a likely option in standard care.”

Where did PCOR Come From?

**Comparative Effectiveness Research Act of 2008**

CER is research “evaluating and comparing the implications and outcomes of two or more health care strategies to address a particular medical condition.”

*(failed to pass)*

**American Recovery and Reinvestment Act of 2009**

Funding for…”**comparative effectiveness** of health care treatments and strategies, through efforts that: (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions

**Patient Protection and Affordable Care Act 2010**

“Patient Centered Outcomes Research Institute established under section 1181(b) of the Social Security Act (referred to in this section as the ‘Institute’) and other government-funded research relevant to comparative clinical effectiveness research”
PCOR and Rare Diseases

“(iii) EXPERT ADVISORY PANEL FOR RARE DISEASE.— In the case of a research study for rare disease, the Institute shall appoint an expert advisory panel for purposes of assisting in the design of the research study and determining the relative value and feasibility of conducting the research study.

**Populations of Interest**

We pay particular attention to a number of populations in making research funding decisions:

- Racial and ethnic minorities
- Older adults
- Low-Income
- Residents of rural areas
- Women
- Children
- Individuals with special healthcare needs, including individuals with disabilities, individuals with multiple chronic diseases, individuals with rare diseases, and individuals whose genetic makeup affects their medical outcomes
- Patients with low health literacy/numeracy and limited English proficiency
- Lesbian, gay, bisexual, transgender (LGBT) persons
- Veterans and members of the armed forces and their families
Patient - ?

Patient/people –
• Centered
• Centric
• Directed
• Driven
• Focused
Patient - ?

Patient/people –
- Centered
- Centric
- Directed
- Driven
- Focused
- Scented?
The **Right Outcomes**

- Once researchers and patients decide on a study question, what is the outcome that makes sense?
- What are meaningful outcomes to *patients*?
Terms/Definitions

**Patient-Reported Outcome:** A report that comes from the patient about the status of a patient’s health condition without amendment or interpretation of the patient’s report by a clinician or anyone else. -- FDA

**Patient-Centered Outcomes:** Those outcomes important to a patient’s survival, function, or feelings as identified or affirmed by patients themselves, or judged to be in the patient’s best interest by providers and caregivers -- Donald Patrick

**Patient-Centered Outcomes Research:** A new research field that considers patients’ needs and preferences, and focuses on the outcomes most important to them -- PCORI
So, to be clear....

Not all PATIENT-REPORTED OUTCOMES are patient centered.

Not all PATIENT-CENTERED OUTCOMES are patient reported.
Patient-Focused Drug Development

An initiative from the Food and Drug Administration (FDA) intended to bring patient perspectives into an earlier stage of product development. The goal is that patients will be able to provide context for benefit-risk assessments and input to review divisions, and also aid in the development of new assessment tools, study endpoints, and risk communications.

FDA activities within PFDD are limited right now to gaining patient insights through 20 disease-specific meetings.

Patient-Centered Versus Patient Engagement

**Patient centeredness** “encompasses qualities of compassion, empathy, and responsiveness to the needs, values, and expressed preferences of the individual patient.” - National Healthcare Disparities Report, 2010 (1)

**Patient engagement** – “meaningful involvement of patients, caregivers, clinicians, and other healthcare stakeholders throughout the research process—from topic selection through design and conduct of research to dissemination of results.” (2)

(2) [http://www.pcori.org/funding-opportunities/what-we-mean-engagement](http://www.pcori.org/funding-opportunities/what-we-mean-engagement)
Definition of PCOR for the Rare-Disease Community

• Scientific investigation that
  • leverages partnership with patients,
  • facilitates a fully comprehensive approach to hearing and heeding the patient's voice throughout the entire research continuum and,
  • uses methods to engage patients beginning at the earliest stages to target what is most meaningful to them.
• The patient voice is central
  • whether it is basic discovery, research and development, the regulatory process, or treatment use,
  • carrying through to healthcare delivery decisions in real-world care, and
• includes comparative-effectiveness considerations.
Study Characteristics:  
PCORI Engagement Rubric

1. **PLANNING THE STUDY:** Describe how patient and stakeholder partners will participate in study planning and design.

2. **CONDUCTING THE STUDY:** Describe how patient and stakeholder partners will participate in the study conduct.

3. **DISSEMINATING THE STUDY RESULTS:** Describe how patient and stakeholder partners will be involved in plans to disseminate study findings and to ensure that findings are communicated in understandable, usable ways.

Study Methods: PCORI Methodology Report

• Cross-Cutting Standards for PCOR:
  • Formulating Research Questions
  • Associated with Patient-Centeredness
  • Data Integrity and Rigorous Analyses
  • Heterogeneity of Treatment Effects

Study Design

Standards for Specific Study Designs and Methods

- Data Registries
- Data Networks as Research-Facilitating Structures
- Causal Inference
- Adaptive and Bayesian Trials
- Studies of Diagnostic Tests
- Systematic Reviews

Traditional Randomized Controlled Trial

Sample

Inclusion criteria

Exclusion criteria

Randomization to groups

Nonparticipants

Enrollment

Intervention group

Allocation

Control group

Loss to follow up

Analysis

Measure outcome

Measure outcome
A PCOR Study Example

1. Patient Survey: Research Priorities
2. Develop Patient Partner Committee (PPC)
3. Sample
4. Randomization to groups
   - Comparator Group A
   - Comparator Group B
   - Nonparticipants
5. Loss to follow up
6. Measure outcome
7. Analyze/Interpret
8. Execute Dissemination Plan

Inclusion criteria
Exclusion criteria

Hydrocephalus Association:
A Randomized Controlled Trial of Anterior vs Posterior Entry Site for Cerebrospinal Fluid Shunt Insertion
End of Study

100% Accrual

75%

50%

25%

2014

2015

2016

2017

2018

2019

Patient Survey:
Research Priorities

Start: Steering Comm. (weekly)

Individual PPC Member Involvement: weekly Steering Committee meetings, Investigator Committee Meetings

Outreach to whole community: conference presentation, webinars, web posts, blogs

Whole PPC Involvement

Study Progress

Abbreviations: Dissemination (Dissem.); Investigator Committee (Invest. Comm.); Patient Partner Committee (PPC)

Hydrocephalus Association, A Randomized Controlled Trial of Anterior vs Posterior Entry Site for Cerebrospinal Fluid Shunt Insertion, Study Timeline
Case Example: National PKU Alliance
National PKU Alliance

• Rare-disease patient advocacy organization
• Created by 18 state and regional support groups across the country
• Vision:
  • To help change the future of PKU--how it will be known, how it will be experience, and how it will be cured
  • Aims to improve the lives of individuals with PKU and to pursue a cure
National PKU Alliance

• Strategic Thinking:
  • Move beyond funding open research
  • Shift towards being an active participant in the development of next generation therapies

• International Scientific Exchange

• Patient Survey on New Treatments
National PKU Alliance: Scientific Exchange

• July 2014 - One day meeting to share research and discuss gaps in knowledge
• 13 lead investigators
• Liver cell transplantation, gene therapy, and PKU brain function
• In and outside PKU
• Share research, discuss challenges, encourage collaboration
• Increase knowledge base
• Held in conjunction with patient conference
National PKU Alliance: Patient Survey

• PKU has a treatment but several challenges with adherence and executive function issues
• Conducted a survey in May 2015 to better understand the current and future needs of the community
• 625 respondents
• Goal: help inform research priorities, provide feedback from patients to medical providers, payers and federal stakeholders, serve as a resource to industry to ensure the patient perspective is central to the development of new therapies
National PKU Alliance: Patient Survey

- 21 Questions
- Current treatment status – therapies, clinic visits, blood phenylalanine levels, difficulty in management
- Importance of new treatments
- Types of new treatments – oral, injections, consumption of probiotic, inserting a gene, infusion of cells
- Symptoms or results most desired to alleviate
- Tolerance of side effects
## Partnership Checklist

### MY CHECKLIST FOR A SUCCESSFUL PARTNERSHIP

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<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>Notes</th>
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<tbody>
<tr>
<td>1. Is the research question patient centered?</td>
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<td>2. Can patient engagement improve the research?</td>
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<td>3. Is there a patient-engagement strategy I can contribute to?</td>
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<td>4. As an engaged patient or organization, can I clearly describe what my role would be in the research?</td>
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<td>5. Would it be active engagement?</td>
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<tr>
<td>6. Would patients have any power to contribute toward decisions about the research?</td>
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</tbody>
</table>

Tool to evaluate Case Examples throughout training and after training
Questions / Discussion
Session Resources

Definitions of Patient-Centered Outcomes Research:
- Establishing the Definition of PCOR: [http://www.pcori.org/establishing-definition-patient-centered-outcomes-research](http://www.pcori.org/establishing-definition-patient-centered-outcomes-research)
- PCORI’s definition of PCOR: [http://www.pcori.org/research-results/patient-centered-outcomes-research](http://www.pcori.org/research-results/patient-centered-outcomes-research)
- PATIENTS definition of PCOR: [http://www.patients.umaryland.edu/pcor/](http://www.patients.umaryland.edu/pcor/)
- CMTP’s definition of PCOR: [http://www.cmtpnet.org/about/patient-centered-outcomes-research/](http://www.cmtpnet.org/about/patient-centered-outcomes-research/)

PCOR vs Traditional Research:
Thank you!