PCORI in Practice: Exploring PCORI's Methodology Standards

July 23, 2014

Patient-Centered Outcomes Research Institute

Today's Presenters

David Hickam, MD

Program Director, Clinical Effectiveness Research
PCORI

Ethan Basch, MD, MSc

Director, Cancer Outcomes Research Program,
University of North Carolina at Chapel Hill
PCORI Methodology Committee Member

Alyce Adams, PhD

Research Scientist II; Section Chief, Health Care Delivery and Policy
Kaiser Permanente Division of Research
Principal Investigator, PCORI-funded study "Balancing Treatment Outcomes and Medication Burden among Patients with Symptomatic Diabetic Peripheral Neuropathy"

Goals for Today

- Gain an understanding of what the Methodology Standards are and why they are important.
- Describe the role of standards in preparing an application and in PCORI merit review.
- Review a current PCORI project as a case study for methods.
- Answer your questions!

About PCORI

pcori.org

Mission

PCORI helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from **research guided by patients, caregivers, and the broader healthcare community.**

pcori
Patient-Centered Outcomes Research Institute

Our Focus

Comparative Clinical Effectiveness Research

- Patient-centered
- Answering questions that matter to patients and other clinical decision makers
- Comparisons of outcomes that matter to patients
- Findings that can be implemented in clinical care environments

Improving Methods for PCOR

Why Do Methods Matter for PCOR?

- Better methods will produce more valid, trustworthy, and useful information that will lead to better healthcare decisions and, ultimately, to improved patient outcomes.

- Methods explain the approach investigators will take to collect data, administer the intervention, and analyze results.

From the Legislation

"The Institute shall establish a standing methodology committee to…develop and improve the science and methods of comparative clinical effectiveness research."

Why Standards?

- In order to fulfill the legislative mandate, the Methodology Committee decided to develop a set of discrete standards that corresponded to different phases of the research process.

What Are the Standards?

- The PCORI Methodology Standards
  - Are guidance for the conduct of PCOR
  - Are minimum requirements
  - Reflect recognized best practices
  - Are supported by scientific evidence
  - Reflect areas where there are deficiencies or inconsistencies in available methods
  - Are NOT comprehensive

Role of the Standards in PCORI Applications

- The Methodology Standards and report are tools for applicants in preparing their applications.
- Applications must demonstrate adherence to PCORI's Methodology Standards.
- Not **all** standards apply to **all** studies.
- The standards do NOT dictate specific study designs.

Role of the Standards in PCORI Merit Review

- The Methodology Standards map to PCORI's merit review criteria.
- PCORI technical reviewers assess the methodological rigor of each study's methods.

PCORI's Methodology Standards

Developing the Methodology Standards

- The Methodology Committee developed the Methodology Standards using a standardized, rigorous process.
- The standards underwent review and revision based on public comments from a wide variety of stakeholders *(July–September 2012).*
- The final report was revised and adopted in December 2013 and became a requirement for all funded projects, starting with the August 2013 Funding Cycle.

47 Individual Methodology Standards

Divided into 2 broad categories and 11 subcategories

Cross-Cutting Standards:

- Formulating Research Questions
- Patient-Centeredness
- Data Integrity and Rigorous Analyses
- Preventing/Handling Missing Data
- Heterogeneity of Treatment Effects

Standards for Specific Designs:

- Data Networks
- Data Registries
- Adaptive and Bayesian Trial Designs
- Causal Inference
- Studies of Diagnostic Tests
- Systematic Reviews

Intention of the Standards

- Are minimal standards for performing comparative effectiveness research
- Are intended to provide helpful guidance to researchers and those who use research results
- Reflect generally accepted best practices
- Provide guidance for both project protocols and results reporting
- Are used to assess the scientific rigor of funding applications
- Context of research should drive use of the standards

The Standards Help to Craft a Research Question

RQ-1 Identify gaps in evidence

Gap analysis and systematic reviews should be used to support the need for a proposed study. If a systematic review is not available, a systematic review should be performed using accepted standards in the field (see standard SR-1), or a strong rationale should be presented for proceeding without a systematic review. In the case where a systematic review is not possible, the methods used to review the literature should be explained and justified.

RQ-6 Measure outcomes that people representing the population of interest notice and care about

Identify and include outcomes the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform an identified health decision. Define outcomes clearly, especially for complex conditions or outcomes that may not have established clinical criteria. Provide information that supports the selection of outcomes as meeting the criteria of "patient-centered," and "relevant to decision makers" such as patient and decision maker input from meetings, surveys, or published studies. Select outcomes based on input directly elicited from patient informants, people representative of the population of interest, either in previous studies or in the proposed research.

The Standards Guide Development of Patient-Centered Projects

PC-2 Identify, select, recruit, and retain study participants representative of the spectrum of the population of interest and ensure that data are collected thoroughly and systematically from all study participants

PC-3 Use patient-reported outcomes when patients or people at risk of a condition are the best source of information

The Standards Address Missing Data

MD-1 Describe methods to prevent and monitor missing data

MD-3 Use validated methods to deal with missing data that properly account for statistical uncertainty due to missingness

The Standards Provide Guidance for Specific Data Collection Methods

DR-1 Requirements for the design and features of registries

A. Patient Follow-up
B. Data Safety and Security
C. Data Quality Assurance
D. Document and Explain Any Modification to the Protocol
E. Consistent Data Collection
F. Systematic Patient Enrollment and Follow-up
G. Monitor and Minimize Loss to Follow-up
H. Collect Data to Address Confounding

DN-1 Requirements for the design and features of data networks

The Report Includes Patient Stories

The report contains four types of stories, each with a different focus.

Stories Highlight Important Methods Issues

RESEARCH IN PRACTICE: Missing Data

Courtney Schreiber, MD, MPH, is a gynecologist and clinical researcher at the University of Pennsylvania School of Medicine. Here she discusses how she uses patient narratives to learn more about how to tailor her studies to the needs of patients. She also uses her patient stories to help recruit and retain enrollees in clinical trials.

How do you talk about missing data with patients?

Schreiber: I often tell a story about a participant named Sally. She enrolled in one of our contraceptive clinical trials. She was absolutely committed to helping women like herself figure out which type of contraception is best. But, after a while, she stopped coming to her study appointments for a logistical reason. When we called her up, she had no idea that dropping out of the study would make it harder for us to learn which medicine worked best. She knew that other women were waiting to enroll in the study, so she thought that someone could just take her spot.

Did Sally leave the study?

Schreiber: No. We were able to figure out how to get her to her appointments: by keeping the research office open late on Thursday. One of the key factors in keeping Sally was being able to show her how much harder it was for us to figure out which medication worked best if we didn't know how she felt at the end of the study. She had been feeling pretty good and thought we could just use the data we had. But once Sally was able to understand how helpful it was for her to stay on as part of the team, she finished the whole study.

How is Sally's story useful in retaining participants on other studies?

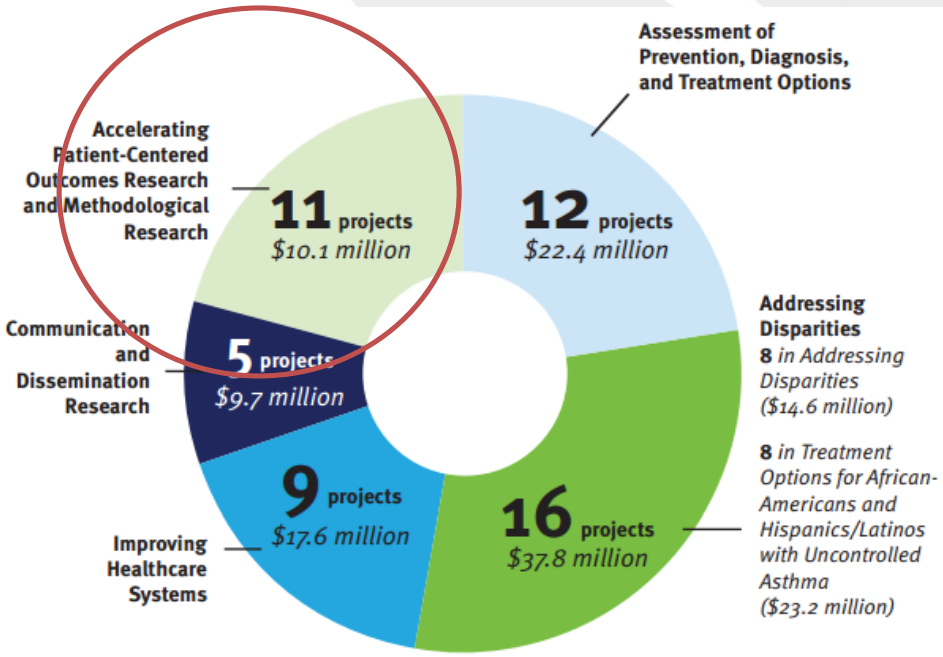
Schreiber: We always promise our study participants that we will work with them to find the most convenient ways to participate, but that message doesn't always stick. But many of them identify with Sally's story, so it helps us explain why staying in the study is so helpful. And it really seems to work.

The stories are not intended to endorse specific research approaches; they demonstrate that good methods make a difference.

The Standards Are Continuously Evolving

PCORI is continuously working to improve the field of methods for PCOR in many ways:

- Funding primary methodological research
- Examining the PCORI portfolio for further methods gaps
- Developing new standards for PCORI and the research community
- Convening experts and hosting workshops on key methods topics
- Disseminating and implementing the Methodology Standards



pcori
Patient-Centered Outcomes Research Institute

The Standards in Practice

Balancing Treatment Outcomes and Medication Burden among Patients with Symptomatic Diabetic Peripheral Neuropathy

Alyce S. Adams, Romain Neugebauer, Joel Clark, and Eileen Kim

for the Diabetic Peripheral Neuropathy Study Team

July 23, 2014

Acknowledgments

- Research Team
  - Co-Is: Andrea Altschuler, Richard Grant, Julie Schmittdiel, Romain Neugebauer (KPNC); Elizabeth Bayliss (KPCO)
  - Clinician/Operations Stakeholders: Eileen Kim (internal medicine), Joseph Young (internal medicine), Marc Jaffe (endocrinologist), Dan Cheung (pharmacist), Gary Choy (pharmacist), Cynthia Mik (DM care manager), Genevieve Foti (quality and operations support consultant), Manuel Ballesca (health IT)
  - Patient Stakeholders: Bonieta Cook, David Willyoung, Joel Clark
  - Research Staff: Wendy Dyer, Rosa Hippler (KPNC), Jennifer Boggs, Christina Clark, Michael Shainline & the IVR Team (KPCO)
  - Consultants: Brian Callaghan, Lisa Prosser (U Michigan); Eve Wittenburg
  - ISM: Kenrik Duru (UCLA-internal medicine)
- Funder: Patient-Centered Outcomes Research Institute (EGID:7250)
- Timeline: Oct 1, 2013 – Sept 30, 2016

KAISER PERMANENTE®

Prospective Cluster Randomized Trial Design

- Outcomes
  - EuroQOL (NeuroQOL Global Health Survey)
  - Medication Changes, Communication
- Randomization
  - Physician level
- Inclusion/Exclusion Criteria
  - All IM physicians treating DM patients
  - New users of DPN Rx with positive screen for DPN
  - Exclusions: <18; gestational diabetes, substance abuse, or cognitive/dementia; >90 days opioid use in the previous 180 days; no English or Spanish

The Intervention

First DPN Rx triggers patient recruitment and consent

Patient receives 3 automated 5-minute phone calls over 6 months

Patient (T) responds to questions

Report provided to patient's PCP

Improved communication and changes in Rx

Application of PCORI Methods Standards in Practice

- Formulating Research Questions
  - Identification of patient-reported outcomes of relevance
  - The development of the patient-centered research question
- Patient-Centeredness
  - Framework for stakeholder engagement
  - Specific examples of how stakeholders inform the research process
- Data Analysis and Heterogeneity of Treatment Effects
  - A few highlights from analytic plan
  - Pre-specified subgroup analysis

“Perfect Storm”— Opportunity for Scientific Inquiry

- DPN is common, but there is much we do not know.
  - Some patients have symptoms and others do not.
  - There is a significant impact on patient quality of life.
- We don’t know which treatment will work for which patient.
  - All available treatments have side effects.
  - Finding the right treatment requires ongoing communication.
- Neuropathy specific PROs are available but underused.
  - NeuroQOL performed especially well in validation studies.
  - Most RCTs focus on pain and use nonspecific PROs.

Sources: Gordois et al, 2003; Boulton et al, 2005; Sadosky et al, 2013; Jain et al, 2011; Manuscript in progress

Patient Perspectives

Quality of Life

"I just don't feel good. I get upset sometimes when I – you know, every day get up, I'm in pain and can't do the things I want to do without being in pain."

Communication

"He [pharmacist] talked to my endocrinologist about it [gabapentin], and they put me on it, and...just really helped...But it wasn't enough by itself. They stopped the amitriptyline, but then, the combination of them is what's working."

"She's [patient's doctor] not too, I guess, receptive to what – to what's important to me."

Patients emphasized the need for more research and that they would welcome regular telephone check-ins via person or computer to communicate about symptoms and side effects.

Sources: Manuscript in progress

Findings from Clinician Stakeholder Meeting

- There is a lack of evidence to guide treatment decision making
- Short clinic visits may hinder communication
- Patients have information that is critical to treatment decision making, but this information is not readily accessible to the doctor at the time treatment decisions are made

Research Question

- A 67-year-old woman with DPN is prescribed a tricyclic antidepressant after nearly 8 months of persistent pain that interferes with her ability to sleep. Soon after starting treatment, she begins to experience dizziness that she believes is caused by her new drug and is considering stopping treatment.

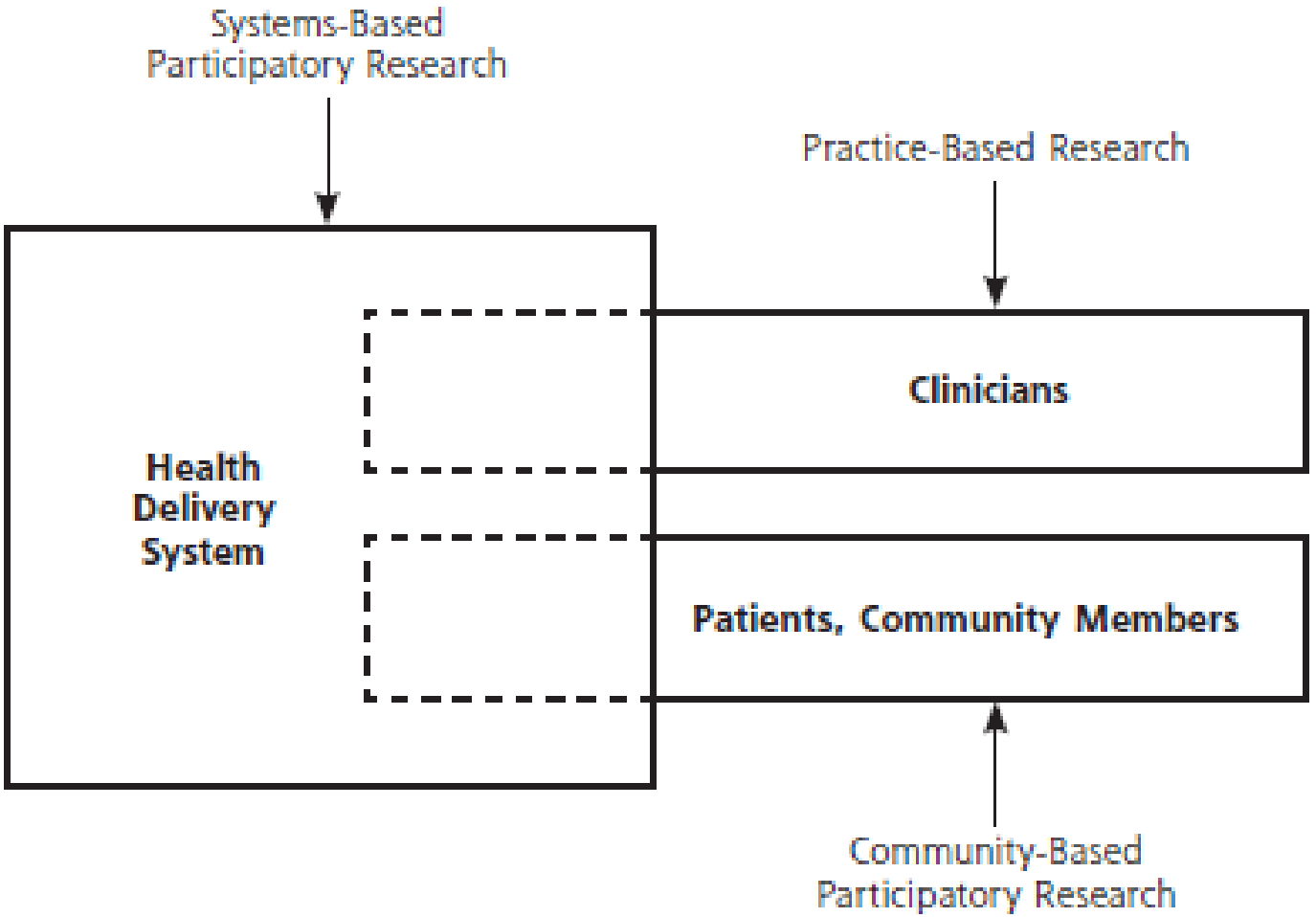
Hypothesis

Systematic collection and feedback of patient-reported data on DPN outcomes to primary care physicians will facilitate appropriate treatment changes that improve patient outcomes.

KAISER PERMANENTE®

Stakeholder Engagement Strategy

Figure 1. Engaging communities in system-based participatory research.



Source: Schmittdiel, Grumbach, Selby, Ann Fam Med (2010)

Ongoing Stakeholder Engagement: Examples from the Field

- Clarity of Study Materials
  - Patient stakeholder review of all patient-facing materials
  - Scope of questions and opportunities for patient feedback
- Intervention Design
  - IVR script
  - Feedback of information to clinicians

Data Analysis and Heterogeneity of Treatment Effects

Data Analysis and Treatment Heterogeneity

- Evaluating the effect of the intervention on quality of life
  - Pre-validated primary outcome
  - GEE to address clustered nature of data
  - Evaluate success of randomization
  - Differential drop-out
- Exploratory HTE analysis
  - Variation in side effect tolerance and shared decision making
  - Conjoint analysis task (subgroup)

Application of the Methods Standards: Lessons Learned

- Standards provide guidance while maintaining flexibility.
  - Do not dictate a particular study design
  - Identify common threats to validity (e.g., ascertainment bias, confounding)
  - Recognition of uncertainties (e.g., accrual rates, drop-out)
- Formalize requirements for rigorous patient engagement in research.

Thank You! To learn more:

- Contact me
  - Alyce Adams, Chief, Health Care Delivery and Policy Section & Research Scientist, Kaiser Permanente Division of Research, Alyce.S.Adams@kp.org
- PCORI http://www.pcori.org/
- ClinicalTrials.gov: NCT02056431

Q&A

Submit your questions!

Contact Us

info@pcori.org

Have a Question?

General Inquiries

info@pcori.org | (202) 827-7200

Research/Programmatic Questions

sciencequestions@pcori.org | (202) 627-1884

Administrative/Financial/Technical Questions

pfa@pcori.org

Engagement and PCORI Activities

getinvolved@pcori.org

Find Us Online

twitter

YouTube

slideshare

www.pcori.org

pcori
Patient-Centered Outcomes Research Institute

ADDITIONAL SLIDES

Start=Rx0	Consent: CATI-1 (Day-14 to 30)	Baseline: CATI-1 (Day-14 to 30)	IVR Call 1 (60 days)	IVR Call 2 (120 days)	IVE Call 3 (180 days)	Follow-up: CATI-2 (210 days)
Informed Consent Form	X					
Demographics	X					
Confirm Rx Start/No Change	X					
Language Preference	X					
Quality of Life		X				X
Pain Interference		X				X
Sleep Interference		X				X
Able to Participate		X				X
Lower Extremity Functioning		X				X
Communication		X				X
Prescribing/Refills		X	X	X	X	X
Shared Decision Making		X				
Treatment Preferences		X				
Patient-Initiated Stopping		X	X	X	X	X
Symptom Changes			X	X	X	
Side Effects			X	X	X	
Communication			X	X	X	