Managing the Mass of Measures: Real People’s Real Data Made Useful
PCORI Methodology Report: Setting the Standard(s) for Rigorous, Patient-Centered Research | June 3, 2014 | 12:00 – 1:00 pm EDT

Presenters:
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David Hickam, Program Director, Clinical Effectiveness Research, Patient-Centered Outcomes Research Institute (PCORI)
The PCORI Methodology Report: Setting the Standard(s) for Rigorous, Patient-Centered Research

Genetic Alliance Standards and Tools Webinar Series
June 3, 2014
Today’s Presenters

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PCORI
About PCORI
pcori.org
PCORI Has a Broad and Complex Mandate

“The purpose of the Institute is to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed through research and evidence synthesis...and the dissemination of research findings with respect to the relative health outcomes, clinical effectiveness, and appropriateness of the medical treatments, services...”

-- from Patient Protection and Affordable Care Act
PCORI helps people make informed health care decisions, and improves health care delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community.
We Engage Stakeholders at Every Step

- Topic Selection and Research Prioritization
- Merit Review
- Evaluation
- Study Design/Implementation
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
What is Patient-Centered Outcomes Research (PCOR)

PCOR helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options.

This work answers patients’ questions.

- **Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?”**
- **What are my options and what are the potential benefits and harms of those options?”**
- **What can I do to improve the outcomes that are most important to me?”**
- **How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?”**
What is a Pragmatic CER Study?

- Assesses whether two or more options differ in effectiveness when administered as they are in real life.
- Project is conducted in a clinical setting that is as close as possible to a real world setting.
- The methodological approach (including study design, outcome measures, and follow-up) is as simple as possible without sacrificing scientific rigor.
PCORI’s Methodology Report
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.
“The Institute shall establish a standing methodology committee to...develop and improve the science and methods of comparative clinical effectiveness research”
Role of Methodology Committee

PCORI’s Methodology Committee (MC) is charged with making recommendations regarding methods for patient-centered outcomes, which includes:

- Guidance about the appropriate use of methods in such research
- Establishing priorities to address gaps in research methods or their application
Developing the Methodology Standards and Translation Table

- Methodology Committee working groups identified and prioritized major methods areas for standards development
- Contractors developed research materials on high priority areas and convened workshops to discuss findings with experts
-External feedback on the translation table through a Request for Information (RFI)
- MC members reviewed, deliberated and ultimately reached consensus on the standards to be included in the report
- MC members reviewed submissions to the RFI and wrote a chapter on the translation table
- The public was invited to submit formal comments on the Methodology Report, on both the standards and translation table
- Based on public comment, the standards and translation table underwent extensive review
- The final report was adopted in December 2013
The Standards are a Requirement for PCORI Funding

Research applications must demonstrate adherence to PCORI’s Methodology Standards.

47 Individual Methodology Standards

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
The Standards are Reasonable and Rigorous

- 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 reporting of results.
- Are used to assess the scientific rigor of funding applications.
- Context of research should drive use of the standards.
- Engage relevant stakeholders in ways that are appropriate and necessary in a given research context.
- Document validated scales and tests.
- Specify plans for data analysis that correspond to major aims.
The Standards Ensure Projects are Patient-Centered

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.

Research proposals and subsequent study reports should describe: 1) the plan to ensure representativeness of participants; 2) how participants are identified, selected, recruited, enrolled, and retained in the study to reduce or address the potential impact of selection bias; 3) efforts employed to maximize adherence to agreed-on enrollment practices; and 4) methods used to ensure unbiased and systematic data collection from all participants.

If the population of interest includes people who are more difficult to identify, recruit, and/or retain than other study populations (for example, individuals historically underrepresented in healthcare research such as those with multiple disease conditions, low literacy, low socioeconomic status, or poor healthcare access, as well as racial and ethnic minority groups and people living in rural areas), then specify plans to address population-unique issues for participant identification, recruitment, and retention.
The Standards Address Missing Data

**MD-1 Describe methods to prevent and monitor missing data**

Investigators should explicitly anticipate potential problems of missing data. The study protocol should contain a section that addresses missing data issues and steps taken in study design and conduct to monitor and limit the impact of missing data. Missingness can occur from patient dropout, failure to provide data, and/or administrative or data management issues. As relevant, the protocol should include the anticipated amount of and reasons for missing data, as well as plans to follow up with participants. This standard applies to all study designs for any type of research question.

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

Statistical inference of intervention effects or measures of association should account for statistical uncertainty attributable to missing data. This means that methods used for imputing missing data should have valid Type I error rates and that confidence intervals should have the nominal coverage properties. This standard applies to all study designs for any type of research question. Bayesian methods and methods such as multiple imputation satisfy this condition, along with various likelihood-based and other validated methods. Single imputation methods like last observation carried forward and baseline observation carried forward are discouraged as the primary approach for handling missing data in the analysis. If investigators do use single-based imputation methods, they must provide a compelling scientific rationale as to why the method is appropriate.
The Standards Provide Guidance for Specific Study Designs

9. Standards for Adaptive and Bayesian Trial Designs

AT-1 Specify planned adaptations and primary analysis

The adaptive clinical trial design should be prospectively planned and the design clearly documented, including:

- All potential adaptations, including timing;
- Trial results and populations that will be used in determining each adaptation;
- Statistical models to be used; and
- Planned analysis of the primary endpoint(s).

The description of the design should be sufficiently detailed that it could be implemented from the description of procedures. The specification of the design should be completed and documented in the trial protocol before enrollment begins. This specification should include, in all but the simplest designs, a statistical analysis plan (SAP) that is separate from the trial protocol in which all necessary detail is provided regarding planned interim and final analyses. Prior specification is a prerequisite for valid and meaningful evaluation of an adaptive design.
The report includes patient stories.

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

- **CER WINS**: Focus on comparative effectiveness research (CER) that led to important changes in clinical practice and patient care.
- **PATIENT VOICES**: Focus on patients who share their own experiences in navigating choices and weighing options.
- **RESEARCH IN PRACTICE**: Focus on the value and challenges of implementing CER.
- **RESEARCH STORIES**: Focus on published research studies that capture the impact that good methodology has on research.
Stories Highlight Important Methods

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

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 Translation Table Outlines Tradeoffs Among Study Designs

The translation table’s purpose is to provide guidance for choosing a basic study design and determining additional design details. The framework in the report comprises the following principles:

- Keep the research and methodology separate.
- Clarify tradeoffs.
- Place individual research studies in the context of a research program.
- Choose study designs taking into account state-of-the-art methodology.
The Translation Framework

Incorporate:
- Prior evidence
- Intent of research and decisions to be made
- Stakeholder perspectives

Specify elements:
- Patient population
- Intervention
- Comparator
- Outcomes
- Timing
- Setting

Determine study characteristics:
- Prioritize study characteristics:
  - Intrinsic
    - Internal validity (bias)
    - External validity
    - Precision
    - Heterogeneity
    - Ethical considerations
    - Others
  - Extrinsic
    - Timeliness
    - Logistical and resource constraints
    - Data availability, quality, and completeness
    - Others

Interface:
- Research Category
  - Therapeutics
  - Diagnostics
  - Evidence Synthesis
  - Other Categories

Translation Table:
- Selection of Study Design
- Methods
- Analytic Approach

Study Execution
Report & Dissemination
Next Steps

The Methodology Committee is continuing to work to improve the field of methods for PCOR in many ways:

- Disseminating and implementing the Methodology Standards to improve methods for all of PCOR.
- Examining the PCORI portfolio for further methods gaps and issues.
- Developing new standards for PCORI and the research community.
- Convening experts and hosting workshops on key methods topics.
How You Can Get Involved

Your feedback is important to our work. The Methodology Committee and PCORI invite you to share your ideas for new standards on our website:

www.pcori.org/research-we-support/methodology/suggest-a-topic-area-for-new-methodology-standards/

For other questions or additional details about PCORI’s Methodology Committee, please email us:

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Have a Question?

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Next Webinar:
Mini-Sentinel | Tuesday, June 17, 12:00 – 1:00 EDT