In-depth look at PCORI's Methodology Standards

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Welcome!

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Session Objectives

- Review the purposes of the Methodology Standards
- Provide an overview of the 11 current categories of standards
- Review how to determine which standards apply to a particular project.

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.

Assessing the Validity of a Study Design

- Internal validity: The basic minimum that permits the data to be adequate for measuring the relationship between interventions and outcomes in the population examined by the study.
- External validity: The ability to generalize the results to other populations of patients.

From the Legislation: PCORI's Methodology Standards

"…Methodologic standards shall provide **specific criteria** for internal validity, generalizability, feasibility, and timeliness of research…[and] shall be scientifically based and include methods by which new information, data, or advances in technology are considered and incorporated into ongoing research projects…"

Developing the Methodology Standards

Methods Selection	• Methodology Committee working groups identified and prioritized major methods areas for standards development
Information Gathering	• Contractors developed research materials on high priority areas and convened workshops to discuss findings with experts
Internal Review	• MC members reached consensus on the standards to be included in the draft report *(May – June 2012)*
External Review	• The public was invited to submit formal comments on the Methodology Report *(July – September 2012)*
Report Generation	• The standards were revised and adopted *(December 2012)* • The final report was revised and adopted *(December 2013)*

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The Methodology Standards are a Tool for Conducting PCOR

The standards fall into 2 broad and 11 specific categories:

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

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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 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 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.

1: Standards for Formulating Research Questions
11: Standards for Systematic Reviews

RQ-1 Identify gaps in evidence

SR-1 Adopt the Institute of Medicine (IOM) standards for systematic reviews of comparative effectiveness research, with some qualifications.

- *A systematic review or gap analysis should justify the need for the study and show that the research question hasn't already been answered*

1: Standards for Formulating Research Questions (cont)

RQ-2 Develop a formal study protocol

RQ-3 Identify specific populations and health decision(s) affected by the research

RQ-4 Identify and assess participant subgroups

RQ-5 Select appropriate interventions and comparators

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

2: Standards Associated with Patient-Centeredness

PC-1 Engage people representing the population of interest and other relevant stakeholders in ways that are appropriate and necessary in a given research context

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

PC-4 Support dissemination and implementation of study results

3: Standards for Data Integrity and Rigorous Analyses

IR-1 Assess data source adequacy

IR-2 Describe data linkage plans, if applicable

IR-3 A priori, specify plans for data analysis that correspond to major aims

IR-4 Document validated scales and tests

IR-5 Use sensitivity analyses to determine the impact of key assumptions

IR-6 Provide sufficient information in reports to allow for assessments of the study's internal and external validity

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4: Standards for Preventing and Handling Missing Data

MD-1 Describe methods to prevent and monitor missing data

MD-2 Describe statistical methods to handle missing data

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

MD-4 Record and report all reasons for dropout and missing data, and account for all patients in report

MD-5 Examine sensitivity of inferences to missing data methods and assumptions, and incorporate into interpretation

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5: Standards for Heterogeneity of Treatment Effects

HT-1 State the goals of HTE analyses

HT-2 For all HTE analyses, pre-specify the analysis plan; for hypothesis-driven HTE analyses, pre-specify hypotheses and supporting evidence base.

HT-3 All HTE claims must be based on appropriate statistical contrasts among groups being compared, such as interaction tests or estimates of differences in treatment effect.

HT-4 For any HTE analysis, report all pre-specified analyses and, at minimum, the number of post-hoc analyses, including all subgroups and outcomes analyzed

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6: Standards for Data Registries
7: Standards for Data Networks as Research-Facilitating Structures

- **DR-1** Requirements for the design and features of registries
- **DR-2** Standards for selection and use of registries
- **DR-3** Robust analysis of confounding factors

- **DN-1** Requirements for the design and features of data networks
- **DN-2** Selection and use of data networks

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8: Standards for Causal Inference

CI-1 Define analysis population using covariate histories

CI-2 Describe population that gave rise to the effect estimate(s)

CI-3 Precisely define the timing of the outcome assessment relative to the initiation and duration of exposure

CI-4 Measure confounders before start of exposure and report data on confounders with study results

CI-5 Report the assumptions underlying the construction of propensity scores and the comparability of the resulting groups in terms of the balance of covariates and overlap

CI-6 Assess the validity of the instrumental variable (i.e. how the assumptions are met) and report the balance of covariates in the groups created by the instrumental variable for all instrumental variable analyses

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9: Standards for Adaptive and Bayesian Trials

AT-1 Specify planned adaptations and primary analysis

AT-2 Evaluate statistical properties of adaptive design

AT-3 Specify structure and analysis plan for Bayesian adaptive randomized clinical trial designs

AT-4 Ensure clinical trial infrastructure is adequate to support planned adaptation(s)

AT-5 Use the CONSORT statement, with modifications, to report adaptive randomized clinical trials

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10: Standards for Studies of Diagnostic Tests

DT-1 Specify clinical context and key elements of diagnostic test study design

DT-2 Study design should be informed by investigations of the clinical context of testing

DT-3 Assess the effect of factors known to affect diagnostic performance and outcomes

DT-4 Structured reporting of diagnostic comparative effectiveness study results

DT-5 Focus studies of diagnostic tests on patient-centered outcomes, using rigorous study designs with preference for randomized controlled trials

Conclusions

- The PCORI Methodology Standards provide useful guidance on the methods for a clinical research project.
- The standards are generally minimal and practical.
- The standards are used for:
  - Review of funding applications
  - Monitoring of project activities
  - Review of final reports

Questions?

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Thank You!

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