Patient-Centered Outcomes Research Institute

PCORI Methodology Committee Report

Setting Standards for Research Methods

August 3, 2012

Presenters

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Executive Director
PCORI

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Lori Frank, PhD
Director,
Engagement Research
PCORI

Webinar Agenda

1. Introduction to PCORI	1:00pm – 1:10pm ET
2. Methodology Committee Mission & Report	1:10pm – 1:20pm ET
3. Research Methods Standards	1:20pm – 1:30pm ET
4. Questions and Answers	1:30pm – 2:00pm ET

Please submit questions for the Q&A portion of today's webinar to **methodswebinar@pcori.org**

Formal public comments can be submitted at **pcori.org/survey/methodology-report/**

Poll Questions 1 - 4

1. **Are you familiar with the contents of the Methodology Committee Report?** (Y/N)

2. **Are you a researcher?** (Y/N)

3. **Rate your understanding of the process the Methodology Committee used to generate standards**:
   a) I do not understand the process the Methodology Committee used to generate standards.
   b) I understand the process somewhat.
   c) I have good understanding of the process the Methodology Committee used to generate standards.

4. **Which response most closely matches your opinion of the Standards in the draft Report?**
   a) The Standards largely cover the main areas important to patient-centered outcomes research.
   b) Several important areas are not covered and additional Standards should be considered.
   c) Don't know/Not sure

About PCORI

- An independent, non-profit organization authorized by Congress.
- Committed to continuously seeking input from patients and a broad range of stakeholders to guide its work.
- Mission – To help people make informed health care decisions and improve 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.**

Defining Patient-Centered Outcomes Research (PCOR)

Helps people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options. This research answers patient-centered questions such as:

Expectations	Options	Outcomes	Decisions
"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 help me make the best decisions about my health and healthcare?"

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PCORI Methodology Committee

MEMBER	TITLE
Sherine Gabriel, MD, MSc (Chair)	Professor of Medicine and of Epidemiology , William J. and Charles H. Mayo Professor at **Mayo Clinic**
Sharon-Lise Normand, MSc, PhD (Vice Chair)	Professor of Health Care Policy (Biostatistics) in the Department of Health Care Policy at **Harvard Medical School** and Professor in the Department of Biostatistics at the Harvard School of Public Health
Naomi Aronson, PhD	Executive Director of the **Blue Cross and Blue Shield Association** Technology Evaluation Center
Ethan Basch, MD, MSc	Associate Attending Physician and Outcomes Scientist at **Memorial Sloan-Kettering Cancer Center**
Alfred Berg, MD, MPH	Professor in the Department of Family Medicine at the **University of Washington** in Seattle
David Flum, MD, MPH	Professor in the Department of Surgery and Adjunct Professor in Health Services and Pharmacy at the **University of Washington** Schools of Medicine, Public Health and Pharmacy
Steven Goodman, MD, PhD	Associate Dean for Clinical and Translational Research, School of Medicine , **Stanford University**
Mark Helfand, MD, MS, MPH	Professor of Medicine and Professor of Medical Informatics and Clinical Epidemiology at the **Oregon Health & Science University**
John Ioannidis, MD, DSc	C.F. Rehnborg Chair in Disease Prevention, Professor of Medicine, Professor of Health Research and Policy, and Director of the **Stanford** Prevention Research Center at Stanford University
Michael Lauer, MD	Director of the Division of Cardiovascular Sciences at the **National Heart, Lung, and Blood Institute**
David Meltzer, MD, PhD	Chief of the Section of Hospital Medicine, The **University of Chicago**
Brian Mittman, PhD	Director, VA Center for Implementation Practice and Research Support, Department of Veterans Affairs **Greater Los Angeles VA Healthcare System**
Robin Newhouse, PhD, RN	Chair and Professor, Organizational Systems and Adult Health at **University of Maryland School of Nursing**
Sebastian Schneeweiss, MD, ScD	Associate Professor of Medicine and Epidemiology at **Harvard** Medical School and Vice Chief of the Division of Pharmacoepidemiology and Pharmacoeconomics at the **Brigham and Women's Hospital**
Jean Slutsky, PA, MSPH	Director of the Center for Outcomes and Evidence , **Agency for Healthcare Research and Quality**
Mary Tinetti, MD	Gladdys Phillips Crofoot Professor of Medicine, Epidemiology, and Public Health in the Division of Geriatrics at **Yale** University School of Medicine
Clyde Yancy, MD, MSc	Chief, Cardiology, **Northwestern** University Feinberg School of Medicine

Methodology Report

- The mandate for PCORI's Methodology Committee is to **define methodological standards** and a **translation table** to guide health care stakeholders towards the best methods for patient-centered outcomes research (PCOR).
- **Rigorous methods** are essential to building trust in research findings.
- The report is the necessary catalyst for **scientifically rigorous**, **patient-centered** outcomes research that can inform decision-making.
- Once Report is revised and accepted by the PCORI Board of Governors, future PCORI funding ***applicants will be expected to reference the Standards in their applications and use the Standards in their PCORI funded research***.

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Methodology Report – Methods Selection

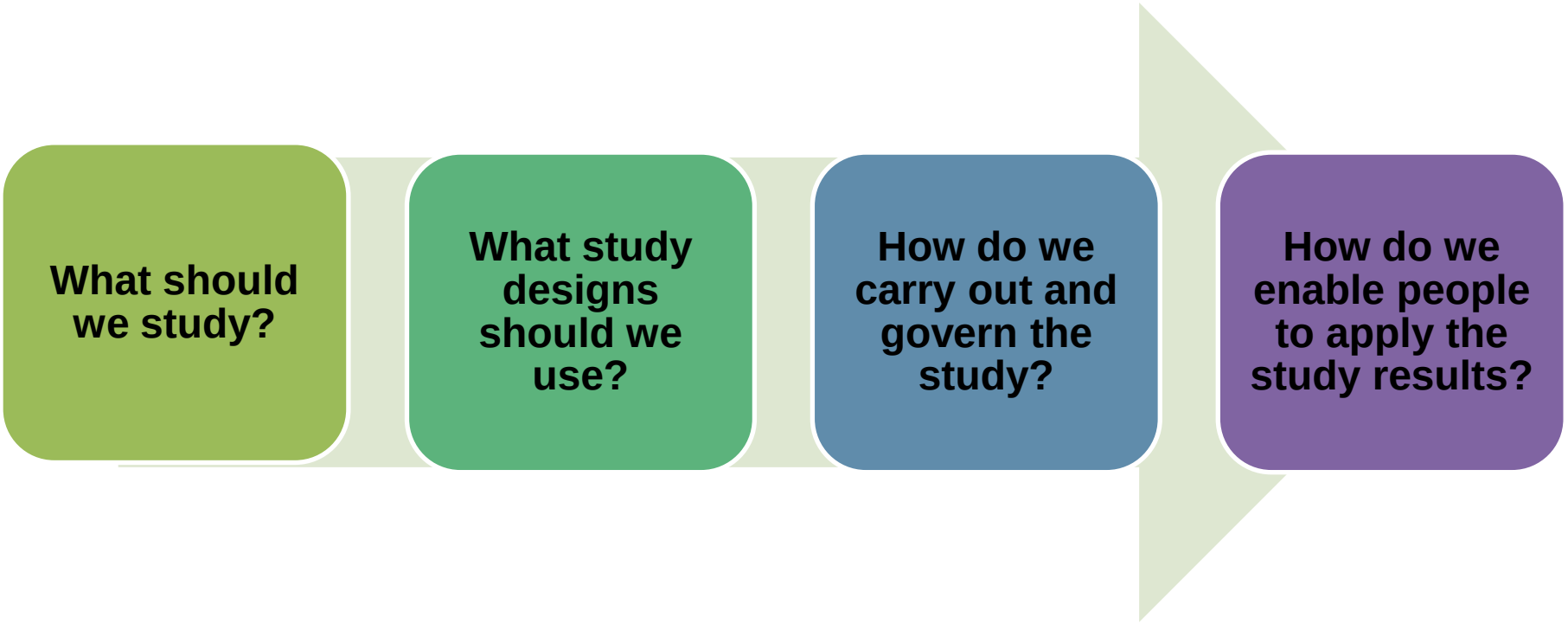
Building on the work of the Institute of Medicine*, the Methodology Committee defined a standard as…

- A process, action, or procedure for performing PCOR that is deemed essential to producing scientifically valid, transparent, and reproducible results; a standard may be supported by scientific evidence, reasonable expectation that the standard helps achieve the anticipated level of quality in PCOR, or by broad acceptance of the practice in PCOR
- The recommendation is actionable, feasible, and implementable
- Proposed standards are intended for use by the PCORI Board, in PCORI policies and procedures, and by PCORI researchers

*Reference: National Research Council. Find What Works in Health Care: Standards for Systematic Reviews. Washington, DC: The National Academies Press; 2011.

Methodology Report – Methods Selection

The MC sought to address selected topics in 4 broad phases of activities in the first Methodology Report:

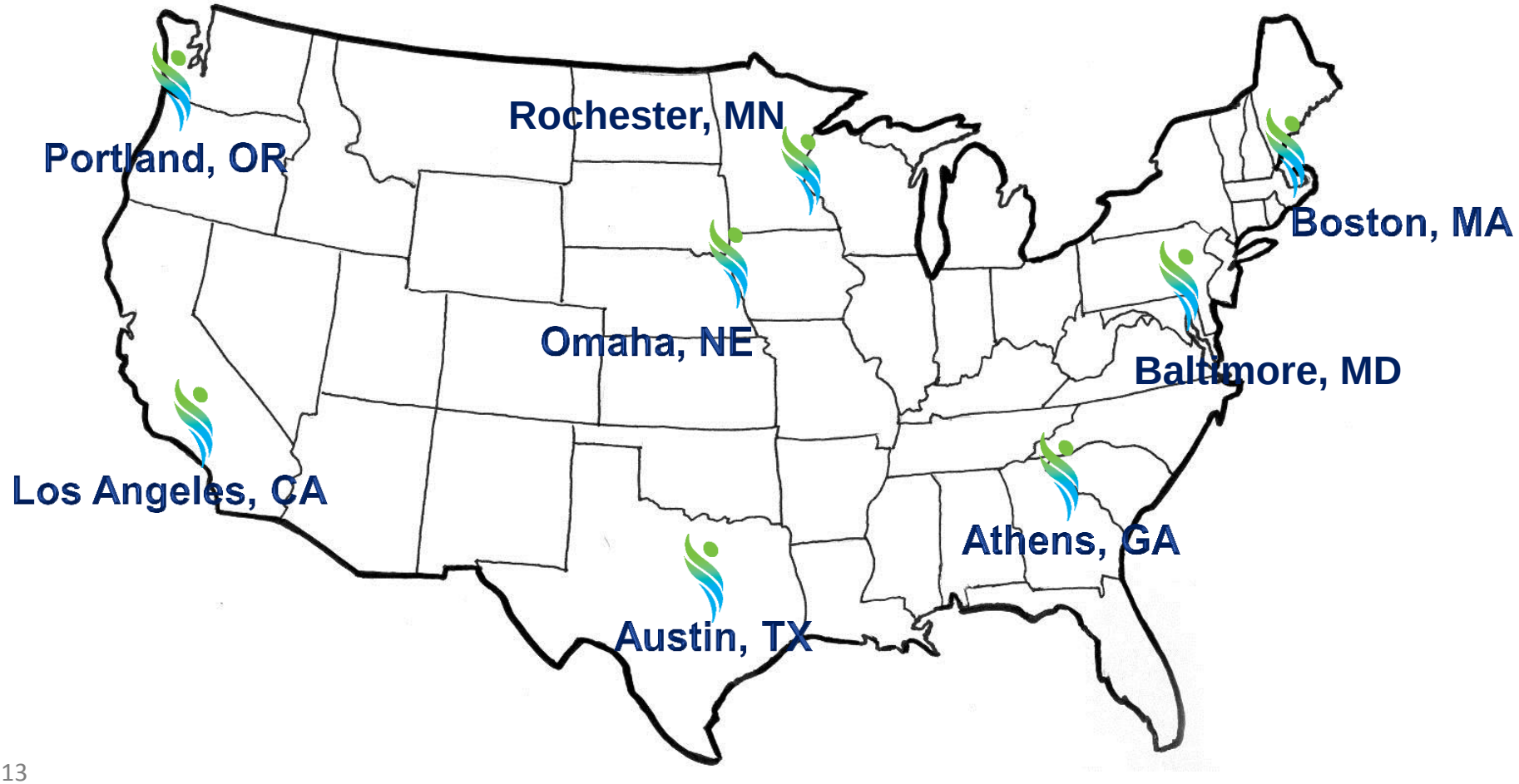


Methodology Report Development

Committee Expertise

1	**Methods Selection**	• Working groups identified and prioritized major research methods questions to be addressed
2	**Information Gathering**	• Researchers contracted to address selected topics • Contractors developed research materials (e.g., reports, summary templates for proposed standard) • MC solicited for external feedback on the translation table (RFI) • Workshops held to discuss contractor findings, with invited experts in attendance
3	**Internal Review**	• MC conducted in-depth internal review of materials developed by contractors, and support staff • MC independently submitted preliminary votes on proposed standards • MC deliberated to reach consensus on recommendations to be endorsed in the report
4	**Report Generation**	• Refined recommendations and report content per committee evaluations and discussions

Methodology Report – Methods Selection

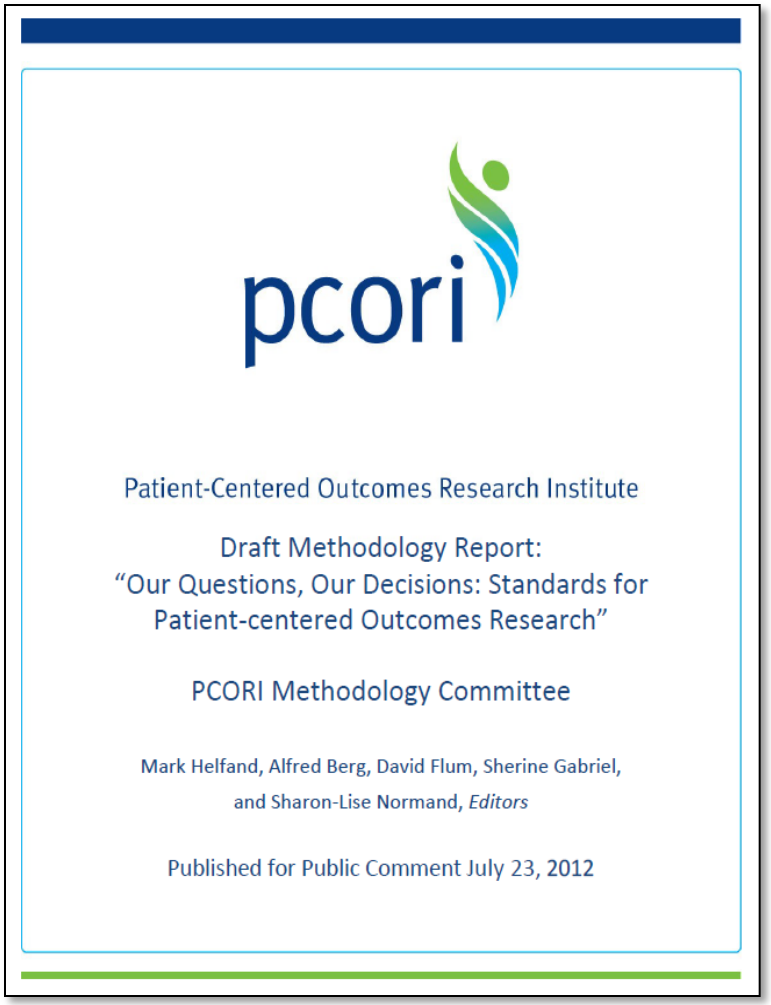


Methodology Report – Internal Review

The MC deliberated and agreed upon standards based on the following:

Patient-Centeredness	Respect for and responsiveness to individual patient preferences, needs, and values
Scientific Rigor	Objectivity, minimizing bias, improving reproducibility, complete reporting
Transparency	Explicit methods, consistent application, public review
Empirical/ Theoretical Basis	Information upon which a proposed standard is based
Other Considerations	Practicality, feasibility, barriers to implementation, and cost

Methodology Report



- Submitted to the PCORI Board of Governors on May 10, 2012
- Accepted by the PCORI Board of Governors on May 21, 2012
- **A public comment period on the draft report: Through September 14 2012**
- Revised Report goes to the Board of Governors November 2012

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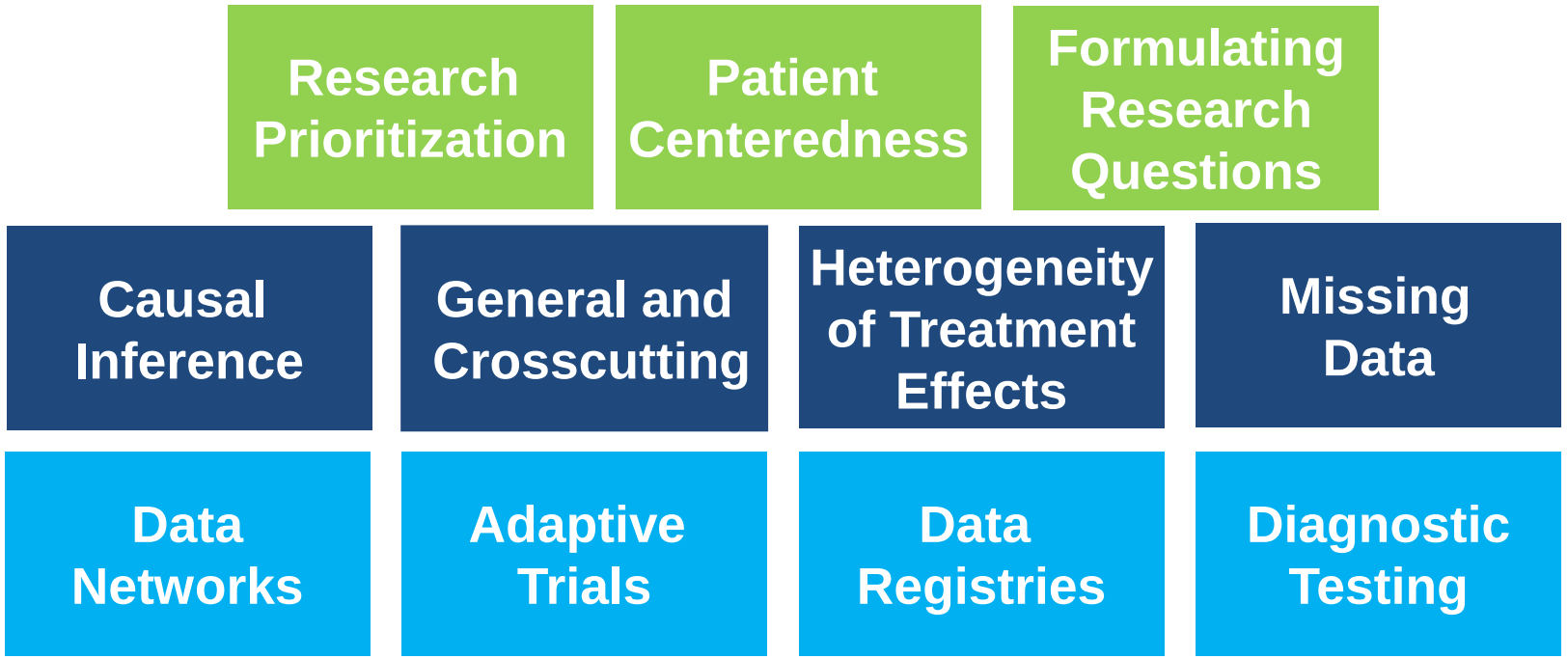
Methodology Report – Research Domains



General Research Standards

3.1.3 Identify and Assess Participant Subgroups

3.1.4 Select Appropriate Interventions and Comparators

7.1.1 Assess Data Source Adequacy

7.1.2 A Priori, Specify Plans for Data Analysis that Correspond to Major Aims

7.1.3 Document Validated Scales and Tests

7.1.4 Use Sensitivity Analyses to Determine the Impact of Key Assumptions

7.1.5 Provide Sufficient Information in Reports to Allow for Assessments of the Study's Internal and External Validity

Causal Inference Standards

7.2.1 Define Analysis Population Using Information Available at Study Entry

7.2.2 Describe Population that Gave Rise to the Effect Estimate(s)

7.2.3 Precisely Define the Timing of the Outcome Assessment Relative to the Initiation and Duration of Intervention

7.2.4 Measure Confounders before Start of Exposure

7.2.5 Assess Propensity Score Balance

7.2.6 Assess Instrumental Variable Assumptions

Heterogeneity of Treatment Effects

- People react differently to treatment
- Problems with summarizing/ averages
  - Answers across lots of types of people are not useful for decisions
  - Do not answer "what will happen to people like me"
- Challenges in dividing patients in 'right' groups

Heterogeneity (HTE) Standards

7.3.1 State the Goals of HTE Analyses

7.3.2 For Confirmatory and Descriptive HTE Analyses, Pre-specify Subgroups and Outcomes; for Confirmatory HTE Analyses, Pre-specify Hypotheses for Each Subgroup Effect

7.3.3 For Confirmatory HTE Analyses, Report a priori Statistical Power

7.3.4 For Any HTE Analysis, Perform an Interaction Test and Report Sufficient Information on Treatment Effect Estimates

7.3.5 For Exploratory HTE Analyses, Discuss Findings in the Context of Study Design and Prior Evidence

7.3.6 For Any HTE Analysis, Report All Pre-specified Analyses and, at Minimum, the Number of Post-hoc Analyses, Including Number of Subgroups and Outcomes Analyzed

Missing Data Standards

7.4.1 Describe in Protocol Methods to Prevent and Monitor Missing Data

7.4.2 Describe Statistical Methods to Handle Missing Data in Protocol

7.4.3 Use Validated Methods to Deal with Missing Data that Properly Account for Statistical Uncertainty Due to Missingness, Such as Multiple Imputation. All Forms of Single Imputation Are Discouraged

7.4.4 Record and Report All Reasons for Dropout and Missing Data, and Account for All Patients in Reports

7.4.5 Examine Sensitivity of Inferences to Missing Data Methods and Assumptions, and Incorporate into Interpretation.

Data Networks

- Explosion of new data
  - Electronic Medical Records (EMRs)
  - Linking data sets
  - New data collection technology

- Need to assure
  - Patient Privacy
  - Data quality
  - Consistency

Data Network Standards

7.5.1 Data Integration Strategy

7.5.2 Risk Assessment Strategy

7.5.3 Identity Management and Authentication of Individual Researchers

7.5.4 Intellectual Property Policies

7.5.5 Standardized Terminology Encoding of Data Content

7.5.6 Metadata Annotation of Data Content

7.5.7 Common Data Model

Adaptive Trials

- Flexible not fixed
  - Adjust based on results that are monitored during study period
- Advantages
  - More relevant
  - Faster results
  - Less expensive (sometimes)
- Challenges
  - Complex to conduct
  - Need to be careful not to introduce bias into the study

Adaptive Trial Standards

8.1.1 Specify Planned Adaptations and Primary Analysis

8.1.2 Evaluate Statistical Properties of Adaptive Design

8.1.3 Specify Structure and Analysis Plan for Bayesian Adaptive Randomized Clinical Trial Designs

8.1.4 Ensure Clinical Trial Infrastructure Is Adequate to Support Planned Adaptation(s)

8.1.5 Use the CONSORT Statement, with Modifications, to Report Adaptive Randomized Clinical Trials

Registries

- Database
  - Information generated during normal care
  - Focused on a disease or treatment
  - Data from multiple sources

- Challenges
  - Privacy
  - Data Quality and Consistency
  - Sorting out cause and effect

Registry Standards

8.2.1 Describe Data Linkage Plans, if Applicable

8.2.2 Plan Follow-up Based on the Registry Objective(s)

8.2.3 Describe Data Safety and Security

8.2.4 Take Appropriate Steps to Ensure Data Quality

8.2.5 Document and Explain Any Modifications to the Protocol

8.2.6 Collect Data Consistently

8.2.7 Enroll and Follow Patients Systematically

8.2.8 Monitor and Take Actions to Keep Loss to Follow-up to an Acceptable Minimum

8.2.9 Use Appropriate Statistical Techniques to Address Confounding

Diagnostic Tests Standards

8.3.1 Specify Clinical Context and Key Elements of Diagnostic Test Study Design

8.3.2 Study Design Should Be Informed by Investigations of the Clinical Context of Testing

8.3.3 Assess the Effect of Factors Known to Affect Diagnostic Performance and Outcomes

8.3.4 Structured Reporting of Diagnostic Comparative Effectiveness Study Results

8.3.5 Give Preference to Randomized Designs of Studies of Test Outcomes

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Poll Questions 5 - 8

5. **Have you ever submitted an application for funding to PCORI? (Y/N)**

6. **Do you plan to submit an application for funding to PCORI in the future? (Y/N)**

7. **Rate your understanding of the process the Methodology Committee used to generate standards:**
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8. **Do you plan to submit comments on the Report through the PCORI website? (Y/N)**

We look forward to your comments on the Draft Methodology Report

- Visit us at www.pcori.org (today's webinar will be archived there)
- Subscribe to PCORI updates at pcori.org/subscribe
- Follow @PCORI on Twitter
- Watch our YouTube channel PCORINews