# A Framework for Patient-Centered Outcomes Research

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# Session Faculty Disclosures

**David H. Hickam, MD, MPH**

- No relevant commercial interests
- No additional disclosures

# Goals for this Presentation

- Review PCORI's model of patient-centered outcomes research
- Describe our approach for ensuring that research projects provide results that are useful for decision makers
- Address the strategies behind the PCORI Methodology Standards
- Address how new research can provide results that are applicable to diverse patient populations

# What is PCORI?

- Established by Congress as part of the Patient Protection and Affordable Care Act
- Our mandate is to develop a program of comparative clinical effectiveness research
  - "Research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of 2 or more medical treatments or services"
  - Improved clinical evidence for decision makers
  - Patient centered outcomes research
- $400 million/year for new projects

# What is PICOTS?

- The **Population** that is studied
- The **Intervention** that is delivered to some patients
- The **Comparator** that other patients receive
- The important patient **Outcomes** that are assessed
- The **Timing** of when outcomes are assessed
- The study's clinical **Setting**

# The PCORI Methodology Standards

- Guidance on the design and conduct of comparative effectiveness research
  - Defined as minimal requirements for good research
  - 47 specific standards grouped in 11 categories

- General domains
  - Ensuring that the research questions are important
  - Engaging participation of patients and research partners
  - Ensuring data validity
  - Specifying appropriate data analyses

# What is Evidence-based Information?

- Clinical evidence: valid data about the outcomes experienced by patients who receive specific clinical interventions
  - The clinical characteristics of the population are well defined and comparable to that of the patients for whom the evidence will be applied
  - The clinical interventions are well defined and reproducible
  - The study measures the right outcomes:  those which are important to patients and their clinicians

# What is the Starting Point of Comparative Effectiveness?

- Examine the choices people make about the options for managing a disease
- Consider how compelling it is to make a choice among these options
- Consider how the need to compare these options could inform the focus of new research
  - Heterogeneity of the patient population
  - Understanding the important benefits and harms
  - Clarity about gaps in the current evidence base
- Engagement with partners facilitates these steps

# Choosing a Study Design: The Problem of Comparability of Groups

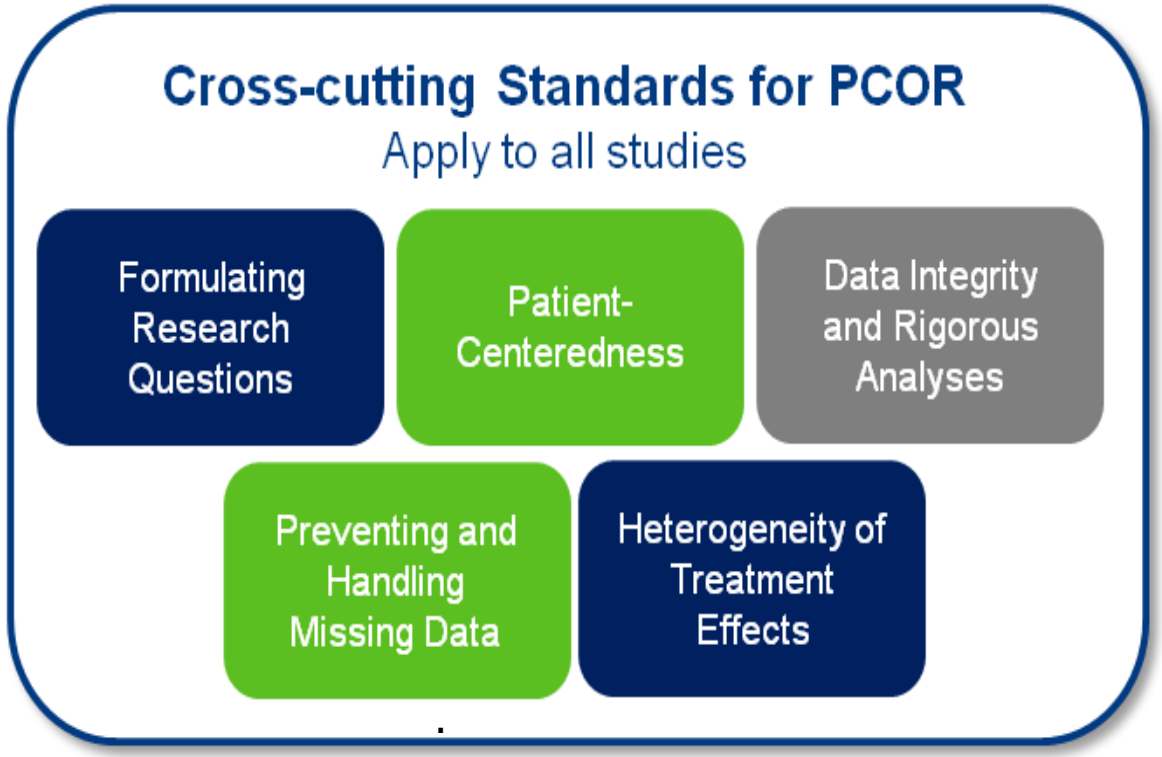
- Confounding: systematic differences between the patients receiving alternative interventions
- Randomization is the best solution but has limitations
  - To include sufficient heterogeneity of the patient population, sample sizes must be quite large
  - Initiatives to streamline the conduct of clinical trials and improve efficiency
- Studies using observational designs can permit evaluation of treatment effect heterogeneity
  - PCORI Methodology Standards
    - Causal inference
    - Heterogeneity of treatment effects

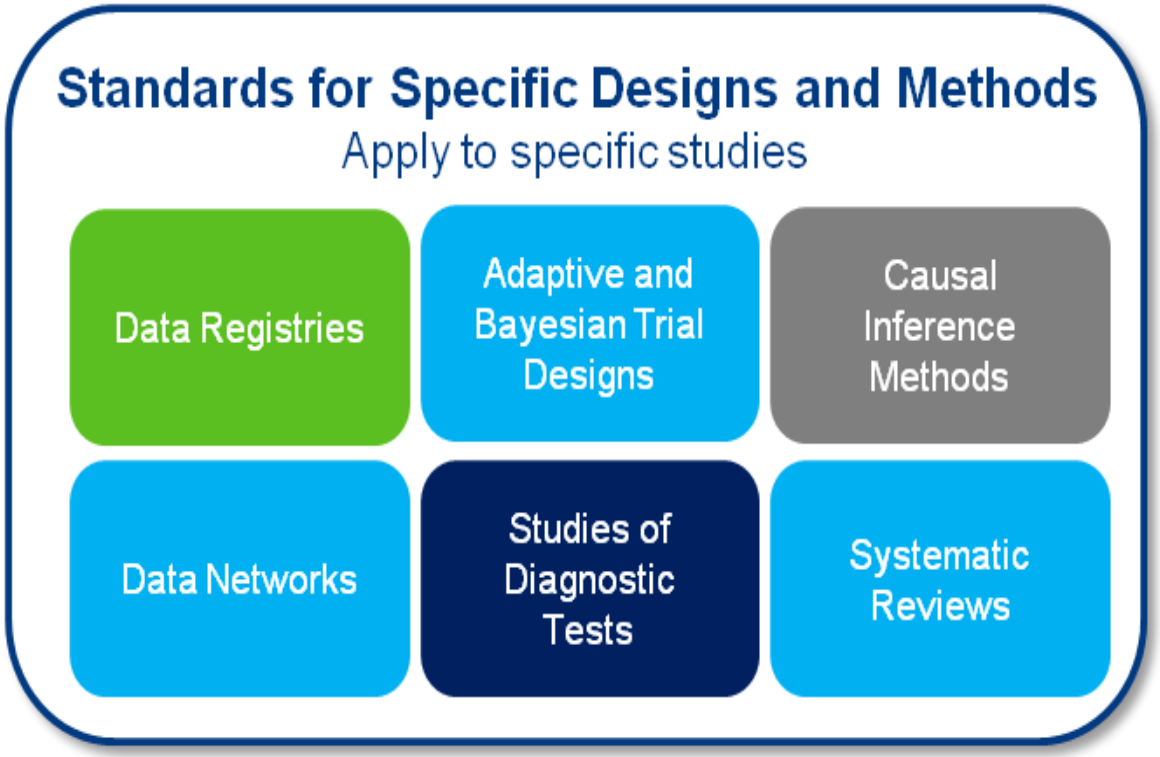
# Choosing the Right Outcomes

- Value of engagement with clinical and patient partners
- Identify the most important benefits and harms
- Patient reported outcomes
  - Can be tailored to those outcomes that are important to patients
  - May require significant infrastructure to obtain these measures
  - Issues of validity of measurement instruments
- Timecourse of measurement: is the follow-up sufficiently long?

# Overview of the PCORI Methodology Standards

The Methodology Committee created 47 Methodology Standards, which fall into 11 categories.



# The Methodology Report Includes Patient Stories

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

# 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.

# 1: Standards for Formulating Research Questions

**RQ-1** Identify gaps in evidence

**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 assessment of the study's internal and external validity

# 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

# 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

# Are there Other important Issues that are not Directly Addressed in the Methodology Standards?

- How to select the best study design to fill an evidence gap: the tradeoff between efficiency and the strength of evidence
- Power and the risk of Type 2 errors: determining the necessary sample size
- How to determine length of follow up: the issue of Timing
- Bias of the research team: the desire to “prove” superiority of a particular clinical practice

# What are Pragmatic Clinical Studies?

- External validity: assessing whether the results of clinical research are applicable to other patient populations
- There are many consideration when planning a new study.
  - Conducting studies in “real world” populations: diversity of the study’s participants
  - Fidelity of delivery of the intervention
  - Assessing outcomes: tradeoffs between direct data collection and using available data about the clinical outcomes
- A more pragmatic study is not always a better study

# Going back to PICOTS

- Research partnerships help in planning several important issues
  - The **Population** that is studied
  - The **Intervention** that is delivered to some patients
  - The **Comparator** that other patients receive
  - The important patient **Outcomes** that are assessed
- Researchers need to plan for other issues:
  - The **Timing** of when outcomes are assessed: how long is long enough?
  - The study's clinical **Setting:** external validity and pragmatic approaches

# Conclusions

- Useful comparative effectiveness research requires careful planning
  - Clarity about the clinical decision that is addressed
  - Identification of an important evidence gap
  - Adherence to best practices:  Methodology Standards
  - Both randomized controlled trials and observational studies can provide valuable evidence
- Planning and carrying out a study is hard
- This research is a partnership between researchers and clinical/patient partners

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# Thank You

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