

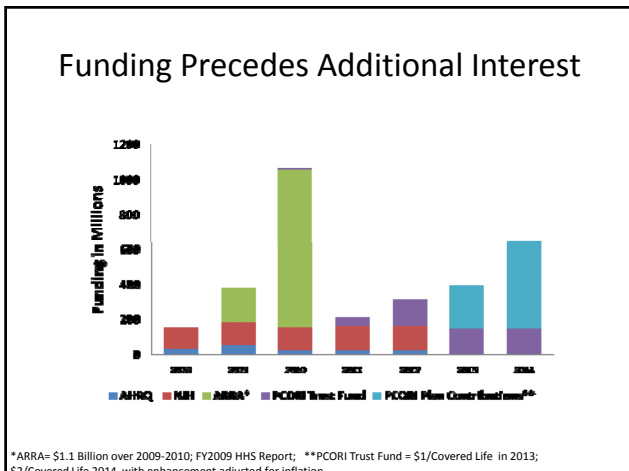
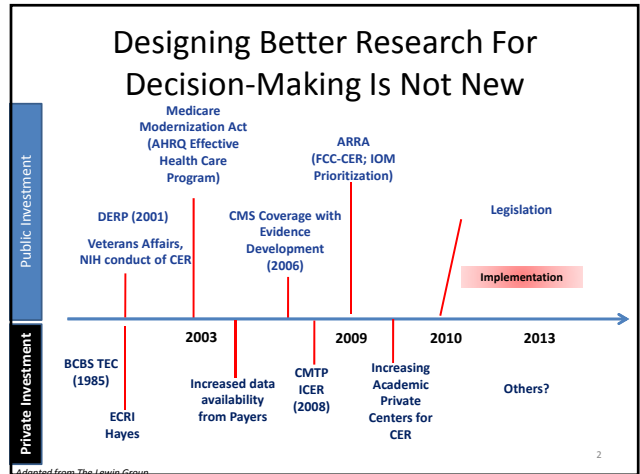
Designing Better Comparative Effectiveness Research

Workshop Session III
November 7, 2011

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PCORI Statute: Call for a translation table

A translation table:
 “designed to provide guidance and act as a reference for the Board to determine research methods that are most likely to address each specific research question.”

Affordable Care Act March 2010, Sec. 6301 Patient Centered Outcomes Research

Methodology Committee Establishment

(A) IN GENERAL

The Institute shall establish a standing methodology committee to carry out the functions described in subparagraph (C).

(C) FUNCTIONS

Subject to subparagraph (D), the methodology committee shall work to develop and improve the science and methods of comparative clinical effectiveness research by, not later than 18 months after the establishment of the Institute, directly or through subcontract, developing and periodically updating the following:

- (i) Methodological standards for research
- (ii) A translation table

Methodological Standards

(C) (i) Methodological Standards for Research

Provide specific criteria for internal validity, generalizability, feasibility, and timeliness of research and for health outcomes measures, risk adjustment, and other relevant aspects of research and assessment with respect to the design of research. Any methodological standards developed and updated shall be scientifically based...

Methodology Committee Structure

Methodology Committee

Co Chairs: Sherine Gabriel, MD, Mayo Clinic & Sharon-Lise Normand, PhD, Harvard Medical School

Report Assimilation

Patient-Centeredness

Methods to incorporate the patient perspective into all phases of PCOR

Research Prioritization

Methods to inform prioritization of new research studies

Research Methods

Methods for using data, design, and statistical analyses to conduct PCOR

Research Methods: Progress to Date

Question: condition, population, treatment & comparator, outcomes, setting

Translation Table Dimensions

Intrinsic Factors

- Internal validity (aka bias)
- External validity (aka generalizability, transportability)
- Precision
- Heterogeneity in risk or benefit (aka "personalized" evidence)
- Ethical dimensions

Extrinsic Factors

- Timeliness (Rapidly changing technology, policy urgency)
- Logistical burden (e.g. study size, complexity, cost)
- Constraints (Data availability, randomization possible?)

Format for Methods Standards / Recommendations

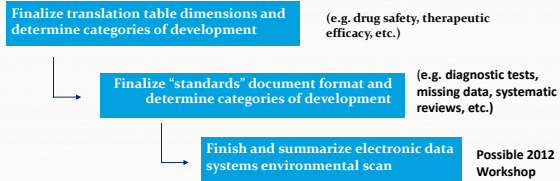
Approaches

- Method
- Key sources
- Major recommendations
- PCORI MC commentary
- Published examples
- Tools for researchers

Sample of Topics

- Heterogeneity
- Missing data
- Involving patients
- Pragmatic trials
- Adaptive trials
- Diagnostic testing
- Systems interventions
- Observational and registry data
- Collaborative data networks

Research Methods: Next Steps

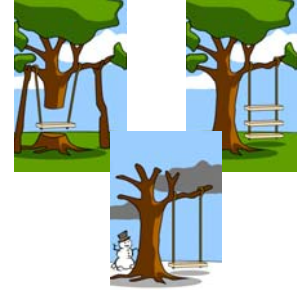


Research and Decision-Making

The study decision-makers need



The studies decision-makers get



Comparative Effectiveness Research

IOM Definition:

The generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.

The CER Hypothesis

- Decision makers (patients, consumers, clinicians, payers, policy makers) should have greater influence in guiding the activities of the clinical research enterprise

Compromise on Methods

- Many CER studies will require a conscious decision to sacrifice internal validity in order to increase generalizability, relevance, feasibility and timeliness
- The right balance is not a scientific issue, it's a social judgment about an acceptable level of uncertainty, involving multiple stakeholders
- Process to achieve this not yet well defined

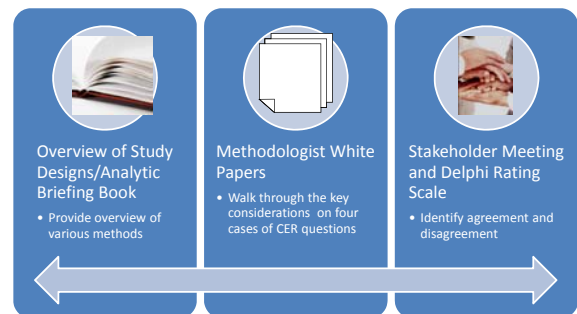
The Great Divide



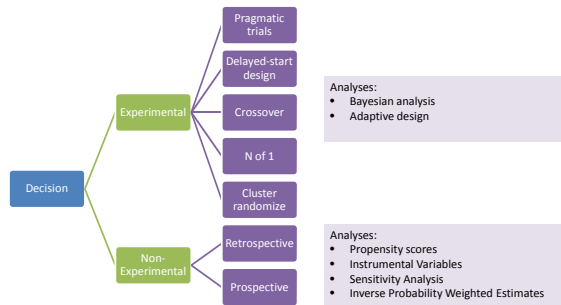
Translation Table Project Goals

- Create a set of guiding principles to help identify appropriate CER study designs and research methods based on specific features or characteristics of the CER study question
- Inform the work of the methodology committee in responding to its mandate
- Provide a framework for designing studies for end-users decision-making

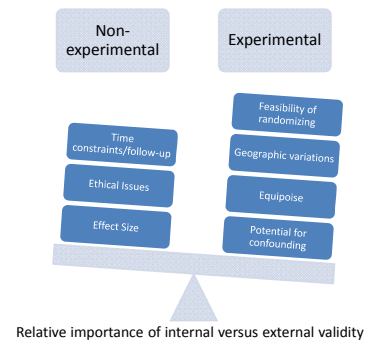
Our Current Effort



Proposed Study Algorithm



Trade-offs and considerations



Other Tradeoffs

- Resource Use
 - Short-term vs. long-term outcomes
 - Study size
 - Subgroup analysis vs. large simple trial
- Availability of data
- Ease of accrual of subjects

Four Cases for White Papers

Cases

- Surgery vs. Radiation Therapy for Localized Prostate Cancer
- Optimal imaging strategy for urolithiasis
- Effectiveness of anticoagulant therapies with hip or knee arthroplasty surgery
- Effectiveness of comprehensive care co-ordination programs, such as the medical home, and usual care in managing children and adults with severe chronic disease

Issues to consider:

- Who are the relevant stakeholders?
- What is the decision meant to be informed by the research question? (Treatment of patient? Reimbursement by payer?)
- Within those parameters, what is best methodological approach to answering questions?

Case Study 1: Prostate Cancer CER

- What is the optimal study design to study the comparative effectiveness of surgery and radiation for localized prostate cancer, by focusing on modern technologies and controlling for differences in patients and treatments that may affect outcomes?

Case Study 1: Prostate Cancer

Therapy Background

- Screening is typically early with PSA
- 10 year Survival is 90%
- Radical prostatectomy is SOC despite significant side effects (urinary incontinence and permanent impotence)
- Alternative: multiple forms of radiotherapy side effects (acute fatigue and diarrhea to durable bowel or urinary problems)
- Potential treatment bias by age
- Administration and doses of radiotherapy vary
- Patient specific parameters are associated with mortality (e.g., black males, or smoking) have higher mortality

Key Gaps

- Head-to-head comparisons of efficacy of new technologies
- Comparison of active interventions to watchful waiting
- Adverse effects of treatment as primary outcomes of studies
- Long-term QoL effects;
- Subgroups - individualized treatment decision-making

Case Study 2: Urolithiasis

- What is the optimal imaging strategy for patients seen in an emergency department with symptoms consistent with urolithiasis (kidney stones)?

Case Study 2: Kidney Stones

Issues	CT	US
Radiation exposure	++++	-
Speed of completion	++	±
Skill required to conduct and interpret	±	+++
Incidentalomas found	+++	±
Cost of the test itself	++++	±
Financial incentives to use test	+++	±
Over-detection and false positives	+++	±
Under-detection and false negatives	±	++

Key Gaps

- CT has increasing popularity, but no randomized trials or prospective trials of ultrasound vs. CT
- No prospective studies comparing diagnosis methods
- Subgroups or subtypes of stones that are diagnosed with greater sensitivity or specificity?
- Does subtype of stone determine treatment strategy?

Case Study 3: Anticoagulant Therapies

- What is the optimal study design to compare the effectiveness of anticoagulant therapies (e.g., low-intensity warfarin, aspirin, injectable anticoagulants) for patients undergoing hip or knee arthroplasty surgery?

Case Study 3: Anticoagulant therapies to prevent venous thromboembolism (VTE)

Approach	Effective?	Lab Monitoring?	Orally available?
Pentasaccharides	Yes	No	No – need daily injection
Low molecular wt heparins	Yes	No	No – need daily injection
Vitamin K antagonist	Less so than for other methods	Yes	Yes

- Other evidence suggest aspirin in combination with pneumatic compression reduces all-cause mortality

Evidence Gaps:

- Some comparisons of rivaroxiban to enoxaparin (a low MW heparin)
- Several new products (e.g., oral direct factor Xa inhibitors) may be similar or more effective than older agents w/similar rates of bleeding
- Few studies evaluating benefits and risks in practice given adherence to medication, monitoring and risks, routine practice of pneumatic compression

Case 4: Care of Chronic Diseases

- Compare the effectiveness of comprehensive care coordination programs, such as the medical home, and usual care in managing children and adults with severe chronic disease, especially in populations with known health disparities.
- (Patient-centered medical home is “an enhanced model of primary care in which care teams, led by a primary care provider, attend to the multifaceted needs of patients and provide whole-person, comprehensive, coordinated, and patient-centered care”)

Case 4: Care of Chronic Diseases

Background

- How to identify patient centered medical home:
 - 1) certification
 - 2) practice-based (fidelity to a set of indicators)
- Indicators: use of health information technology & EMR, electronic access to clinical information from specialists and hospitals, electronic prescribing, use of chronic disease registries, incorporation of patient feedback, guideline based reminders, and use of emails for patient-physician communication.

Key Gaps

- Most data analyses have been retrospective observational
- Limited in their ability to describe the characteristics of a practice and how that changes over time.
- Studies have been subject to selection bias both on the part of the plans and of patients enrolled in those plans.
- There are limited data on impact on patient satisfaction and quality of life.



Thank you