COMPARATIVE EFFECTIVENESS RESEARCH: NOT JUST RED PILL VERSUS BLUE PILL

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Objectives

To understand the role of comparative effectiveness research and outcomes research in improving health
Outline

- Motivating forces
- Recent legislation
- Prominent methodologies
What is CER?

CER is 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.

- Institute of Medicine, 2009
The Problem

“I think there’s a general recognition that the system we have in America is fundamentally broken. We spend more than any country on Earth. Our health results look like we’re a developing nation.”

- Secretary Kathleen Sebelius, HHS

“Better information about the costs and benefits of different treatment options...could eventually lower health care spending...”

- Peter Orszag, Former head of CBO, OMB
Two Big Forces

- Desire to deliver clinical care based on evidence
- Desire to improve effectiveness of care while containing costs
A Drive for Evidence
Early Appreciation of Medical Evidence (late 1980’s)

To ensure high-quality medical care:

- Analyze evidence of the effectiveness, risks and costs of various medical practices (and define appropriateness of these practices)
- Monitor existing practices and compare them against accepted standards
- Change the behavior of practitioners to ensure that care delivered meets the standards

Their recommendations:

• Examine practices and develop practice standards based on evidence
• Estimate the magnitudes of the effects of different options on health and economic outcomes
• Policy statements about practices should keep separate the statements about the estimates of outcomes and the judgments [recommendations] about the practice
• Better coordination of research
• Higher standards for publications
• Higher standards for practice standards (e.g. less expert opinion)
Weak Evidence in Guidelines: Recommendations Based on Randomized Trials

- Atrial fibrillation: 11.7%
- Heart failure: 26.4%
- Peripheral arterial disease: 15.3%
- ST-Elevation-MI: 13.5%
- Perioperative beta-blockers: 12.0%
- Secondary prevention: 22.9%
- Stable angina: 6.4%
- Supraventricular arrhythmias: 6.1%
- Unstable angina: 23.6%
- Valvular disease: 0.3%
- Ventricular arrhythmia: 9.7%
- Percutaneous angioplasty: 11.0%
- Bypass surgery: 19.0%
- Pacemaker: 3.5%
- Radionuclide imaging: 4.8%

Tricoci P et al. *JAMA* 2009
The U.S. Preventive Services Task Force

- First convened by the U.S. Public Health Service in 1984
- Independent panel of private-sector experts in prevention and primary care.
- Conducts rigorous, impartial assessments of the scientific evidence for the effectiveness of a broad range of clinical preventive services

**Mission** is to evaluate the benefits of individual services based on age, gender, and risk factors for disease; make recommendations about which preventive services should be incorporated routinely into primary medical care and for which populations; and identify a research agenda for clinical preventive care.
• An international, non-profit, independent organization, established to ensure that up-to-date, accurate information about the effects of healthcare interventions is readily available worldwide.

• Produces and disseminates systematic reviews of healthcare interventions, and promotes the search for evidence in the form of clinical trials and other studies of the effects of interventions.
Others Leaders in Systematic Reviews of Evidence

• Evidence Based Practice Centers of the Agency for Healthcare Research and Quality (since 1996)

• National Institute for Health and Clinical Effectiveness (U.K., National Health Service) (since 1999)
A Drive for Improving Efficiency of Care Delivery
Advancement of Health Services Research (circa late 1980’s)

• Prompted by John Wennberg’s research on practice variations and Robert Brook’s research at RAND
Age-Adjusted Rates of Procedures For Six Common Surgical Procedures In Rhode Island, Maine, and Vermont (1975)

T & A = tonsillectomy/adenoidectomy
Unsustainable Spending on Healthcare

Projected Spending on Health Care as a Percentage of Gross Domestic Product

Source: Congressional Budget Office.

Note: Amounts for Medicare are net of beneficiaries’ premiums. Amounts for Medicaid are federal spending only.
Wennberg published a call to action --1984

Called for:

• Closer monitoring of medical practices in local hospital markets using epidemiology
• Address unanswered questions about the effectiveness of many common therapeutic interventions (are they beneficial and relatively safe)
• Cost-containment by reducing the use of hospitals for conditions that do not require inpatient treatments

Gains in Health Services Research (late 1980’s)

- Concerns on Capitol Hill about health care costs and viability of Medicare
- William Roper was head of Health Care Financing Administration (HCFA, now CMS) got effectiveness research as an item in proposed FY 1990 budget
- Later as White House health policy advisor advocated for “effectiveness research”

Agency for Healthcare Research and Quality (AHRQ) –1989 (AHCPR)

- Precursor had been National Center for Health Services Research, a program under the assistant secretary for HHS
- Promoted by legislation to be a PHS agency (1989)
- Remarkable change in funding for health services research with this move
Clinton Healthcare Reforms (proposed) 1993

- President Clinton urged Congress "to fix a health care system that is badly broken..."

- Senator Clinton noted “Despite the lack of universal coverage in our country, we still spend much more than countries that provide health care to all their citizens. We are No. 1 in the world in health care spending. On a per capita basis, health spending in the United States is 50 percent higher than the second-highest-spending country: Switzerland.”

- “Our system rewards clinicians for providing more services but not for keeping patients healthier [i.e. delivering effective care].”
2000-2010

- Political environment favoring modernization of health care delivery
- Recognition of the need for *effectiveness* in health care
- Health professionals being trained with increased focus on genomics and informatics (personalization)
- Health research with a focus on balancing effectiveness and safety
Premise: it is possible to constrain health care costs both in the public programs and in the rest of the health system without adverse health consequences.

“Perhaps the most compelling evidence is substantial geographic differences in spending on health care, which do not translate into higher life expectancy or measured improvements in other health statistics in the higher spending regions.”
And yet …

Hard evidence is often *unavailable* about and whether the added *which treatments work best for which patients* benefits of more-effective but more expensive services are sufficient to warrant their added expense.

**Goal of comparative effectiveness research** is to generate better information about the risks and benefits and costs of different treatment options ---- which could eventually alter the way in which medicine is practiced and yield lower health care spending without having adverse effects on health.
Criteria for adoption decisions: sometimes its easy, sometimes not

<table>
<thead>
<tr>
<th>Impact on health</th>
<th>Cost-saving</th>
<th>Cost-Neutral</th>
<th>Cost-Increasing</th>
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<tbody>
<tr>
<td>Higher effectiveness</td>
<td>Adopt (big winner)</td>
<td>Adopt (winner)</td>
<td>Depends on societal willingness to pay</td>
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<tr>
<td>Similar effectiveness</td>
<td>Adopt (winner)</td>
<td></td>
<td>Do not adopt (loser)</td>
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<tr>
<td>Lower effectiveness</td>
<td>Depends on societal willingness to pay</td>
<td>Do not adopt (loser)</td>
<td>Do not adopt (big loser)</td>
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The American Reinvestment and Recovery Act (ARRA) of 2009

Effective February 17, 2009
SEC. 3. PURPOSES AND PRINCIPLES.

(a) STATEMENT OF PURPOSES.—The purposes of this Act include the following:

(1) To preserve and create jobs and promote economic recovery.
(2) To assist those most impacted by the recession.
(3) To provide investments needed to increase economic efficiency by spurring technological advances in science and health.
(4) To invest in transportation, environmental protection, and other infrastructure that will provide long-term economic benefits.
(5) To stabilize State and local government budgets, in order to minimize and avoid reductions in essential services and counterproductive state and local tax increases.
The American Reinvestment and Recovery Act (ARRA)

- ARRA contained $1.1 billion for comparative effectiveness research.
  - $300 million for the Agency for Healthcare Research and Quality (AHRQ)
  - $400 million for the National Institutes of Health (NIH)
  - $400 million at the discretion of the HHS Secretary

- The legislation called on the Institute of Medicine to recommend research priorities for the Secretary's funds
Patient Protection and Affordable Care Act
March 23, 2010

Included: Sec. 6301 Patient Centered Outcomes Research
SEC. 6301. PATIENT-CENTERED OUTCOMES RESEARCH.

(a) IN GENERAL.—Title XI of the Social Security Act (42 U.S.C. 1301 et seq.) is amended by adding at the end the following new part:

“PART D—COMPARATIVE CLINICAL EFFECTIVENESS RESEARCH

“COMPARATIVE CLINICAL EFFECTIVENESS RESEARCH

“Sec. 1181. (a) DEFINITIONS.—In this section:

“(1) BOARD.—The term ‘Board’ means the Board of Governors established under subsection (f).

“(2) COMPARATIVE CLINICAL EFFECTIVENESS RESEARCH; RESEARCH.—

“(A) IN GENERAL.—The terms ‘comparative clinical effectiveness research’ and ‘research’ mean research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of 2 or more medical treatments, services, and items described in subparagraph (B).
Key Items in Sec. 6301

- Establishment of PCORI: Patient-Centered Outcomes Research Institute
- NOT an agency of the government

- Mission: The Patient-Centered Outcomes Research Institute (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.
Is comparative effectiveness research the same as patient-centered outcomes research?
The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed health care decisions and improve health care delivery. PCORI will commission research that is guided by patients, caregivers and the broader health care community and will produce high integrity, evidence-based information.

PCORI is committed to transparency and a rigorous stakeholder-driven process that emphasizes patient engagement. PCORI will use a variety of forums and public comment periods to obtain public input throughout its work.
Duties of PCORI

- Identifying research priorities
- Defining research agenda
- Carrying out research project agenda (largely through contracts)
- Research will take into account differences between patients
- Research will take into account differences in treatments
Structure of PCORI

• An Institute Board of Governors (includes directors of NIH and AHRQ)
• Expert advisory councils
• Methodology committee
• May use processes of another agency
• High priority on transparency
• Will support training activities through AHRQ and NIH mechanisms
Eugene Washington, MD, MSc, Vice Chancellor, UCLA Health Sciences, and Dean, David Geffen School of Medicine, University of California Los Angeles. Dr. Washington will serve as the chair of the PCORI Board of Governors.

Steven Lipstein, MHA, President and Chief Executive Officer, BJC Health Care, a non-profit health care delivery system. Mr. Lipstein will serve as the vice chair of the PCORI Board of Governors.

Christine Goertz, DC, PhD, Vice Chancellor for Research and Health Policy, Palmer College of Chiropractic and Palmer Center for Chiropractic Research.

Sharon Levine, MD, Associate Executive Director for The Permanente Medical Group of Northern California, a large multi-specialty group practice within Kaiser Permanente’s integrated delivery system.

Ellen Sigal, PhD, Chairperson and founder of Friends of Cancer Research, a cancer research think tank and advocacy organization.

Harlan Weisman, MD, Chief Science and Technology Officer, Medical Devices and Diagnostics, for Johnson & Johnson.

Robert Zwolak, MD, PhD, a vascular surgeon at Dartmouth-Hitchcock Medical Center and professor of surgery at the Dartmouth Medical School.

Lawrence Becker, Director, Strategic Partnerships and Alliances, Xerox Corporation.

Arnold Epstein, MD, the John H. Foster Professor and Chair of the Department of Health Policy and Management at Harvard University School of Public Health, and practicing internist at Brigham and Women’s Hospital.
Andrew Imparato, JD, President and Chief Executive Officer of the American Association of People with Disabilities.

Robert Jesse, MD, PhD, Principal Deputy Under Secretary for Health and National Program Director for Cardiology, Department of Veterans Affairs.

Freda Lewis-Hall, MD, Chief Medical Officer and Senior Vice President of the Pfizer Medical Division.

Grayson Norquist, MD, MSPH, Professor and Chairman, Department of Psychiatry and Human Behavior, University of Mississippi Medical Center.

Debra Barksdale, PhD, RN, Associate Professor, University of North Carolina (UNC) at Chapel Hill School of Nursing.

Kerry Barnett, JD, Executive Vice President of Corporate Services and Chief Legal Officer, The Regence Group.

Allen Douma, MD, Chief Executive Officer of Empower, LLC, and a member of the AARP Board of Directors.

Leah Hole-Curry, JD, Program Director for the Health Technology Assessment (HTA) program, Washington State Health Care Authority.

Harlan Krumholz, MD, Harold H. Hines, Jr. Professor of Medicine and Epidemiology and Public Health at Yale University School of Medicine.

Richard E. Kuntz, MD, Senior Vice President and Chief Scientific, Clinical, and Regulatory Officer of Medtronic, Inc.
PCORI - Funding

• Supported by a trust fund

• Up to 20% of the Fund will support research capacity building and dissemination of results

• PCORI will fund research through contracts with federal agencies – primarily AHRQ and NIH (constitutional question as to whether a federal entity can act as a contractor for a non-governmental entity)
“(a) CREATION OF TRUST FUND.—There is established in the Treasury of the United States a trust fund to be known as the ‘Patient-Centered Outcomes Research Trust Fund’ (hereafter in this section referred to as the ‘PCORTF’), consisting of such amounts as may be appropriated or credited to such Trust Fund as provided in this section and section 9602(b).

“(b) TRANSFERS TO FUND.—

“(1) APPROPRIATION.—There are hereby appropriated to the Trust Fund the following:

“(A) For fiscal year 2010, $10,000,000.
“(B) For fiscal year 2011, $50,000,000.
“(C) For fiscal year 2012, $150,000,000.
“(D) For fiscal year 2013—

“(i) an amount equivalent to the net revenues received in the Treasury from the fees imposed under subchapter B of chapter 34 (relating to fees on health insurance and self-insured plans) for such fiscal year; and

“(ii) $150,000,000.

“(i) an amount equivalent to the net revenues received in the Treasury from the fees imposed under subchapter B of chapter 34 (relating to fees on health insurance and self-insured plans) for such fiscal year; and

“(ii) $150,000,000.
The amounts appropriated under subparagraphs (A), (B), (C), (D)(ii), and (E)(ii) shall be transferred from the general fund of the Treasury, from funds not otherwise appropriated.

“(2) TRUST FUND TRANSFERS.—In addition to the amount
PCORI – Methodology Tasks

• Legislation requires the research meets methodological standards for CER

• Separate solicitation for members of the Methods Committee

• Expected that the Methods Committee will consult or contract with Institute of Medicine, Agency for Healthcare Research and Quality (AHRQ), NIH, academics and non-profits, private entities with relevant experience
First Task of Methods Committee: Define PCOR

Patient Centered Outcomes Research (PCOR) helps people make informed health care decisions and allows their voice to be heard in assessing the value of health care options. This research answers patient-focused questions:

“Given my personal characteristics, conditions and preferences, what should I expect will happen to me?”

“What are my options and what are the benefits and harms of those options?”

“What can I do to improve the outcomes that are most important to me?”

“How can the health care system improve my chances of achieving the outcomes I prefer?”
Key Methodologies of CER/PCOR
Types of questions

- Comparative
- Effectiveness
- Patient-centered/patient-relevant
- Stakeholders
Evidence review

• Skills of systematic review of the literature
• Skill of meta-analysis
• Skills to disseminate results of research through clinical practice guidelines/consumer guides/publications in the lay literature
Observational Research

- Difference between efficacy and effectiveness
- Large dataset research to understand effectiveness of therapies in a usual care setting
  - Administrative claims
  - Electronic medical records
  - Registries
Experimental Research

Pragmatic clinical trials

Trials conducted in a usual care setting without tight inclusion and exclusion criteria
Stakeholder Engagement

• Learning better methods for engaging stakeholders in the process of designing research
• Methods for engaging community (clinicians and patients) in participating in research in their usual care setting
Modeling

• Decision-analysis
• Cost analysis (perhaps)
Cost Research (okay?)

- CER provisions in the legislation *do not* prohibit comparative cost effectiveness.
- Act *does* explicitly state that PCORI will not “develop or employ” a dollars per QALY approach to evaluation of interventions.
“The Patient-Centered Outcomes Research Institute … shall not develop or employ a dollars-per-quality-adjusted life year (or similar measure that discounts the value of a life because of an individual’s disability) as a threshold to establish what type of health care is cost-effective or recommended.”
Summary

• Exciting opportunities for improving effectiveness of care and care delivery
• Supportive legislation
• Possibility of more stable funding streams
• Greater transparency in research
• Appreciation of the role of stakeholders in this process