Comparative Effectiveness Research: Opportunities for the Implementation Research Community

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Outline

(1) What is CER?
   (1) Definitions
   (2) Conceptual questions
(2) Why the attention on CER?
   (1) Link to 2009 healthcare reform debate
(3) Current examples of CER
   (1) AHRQ’s Effective Health Program
(4) Role of Implementation Science
   (1) Obvious roles
   (2) Novel opportunities
Disclaimer

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Comparative Effectiveness

“…a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients.”

CBO, 2007
CER Definition Extended

• Compare similar treatments--competing drugs, or different approaches--surgery versus drug therapy
• Analysis may focus on:
  – Relative medical benefits and risks of each option
  – Weigh costs and benefits of those options
• Key issue is determining benefits for different types of patients for a given treatment
• In settings providing same treatment, can address differences in
  – Diagnoses, systems of care, tests and follow-up
CER Bottom-line

• The core question of comparative effectiveness research—which treatment works best, for whom, and under what circumstances—is a fundamental concern for patients and clinicians confronting a health problem.

• The direct comparison of existing health care interventions to determine which works best for which patients and which poses the greatest benefits and harms.
Additional Considerations in Defining CER

• Strength of Evidence
  - What is the minimal level (threshold) of validity needed when comparing treatments?

• Applicability of Evidence
  - How specific to the clinical question does the evidence of effectiveness need to be?
An Important Conceptual Distinction When Defining CER

• Two distinct forms of comparative effectiveness research
  – A comparative effectiveness review
    • Evidence synthesis
  – A comparative effectiveness study
    • Evidence generation
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Why Comparative Effectiveness Research?

• The Federal government has a stake in CER
  - Private sector has limited incentives for CER
  - CER is not generally required for FDA approval as safe and effective
  - The Federal government plays a substantial role in financing health care in the U.S.
  - Obama administration believes CER will play a role in healthcare reform by better aligning benefits, costs & quality

CBO, 2007
Scope of the Opportunity in Health Care Reform

• Major challenges in 21st Century health care include evaluating all innovations and determining which:
  – Represent added value
  – Offer minimal enhancements over existing choices
  – Fail to reach their potential
  – Work for some patients and not for others

(AHRQ, 2008)
Current US Activities in CER

• AHRQ Effective Practice Centers 1998 to present
• AHRQ Effective Health Care Program 2005 to present
  – $30 million in 08-09; $50 million in 2009
• Department of Veterans Affairs (QUERI program)
• Drug Effectiveness Review Project (at OHSU)
• Other agencies: CMS, NIH (limited activities)
• Health plan and other private efforts (including Cochrane Collaboration)
American Recovery and Reinvestment Act 2009 and CER

- **Congress allocated $1.1 Billion for CER:**
  - AHRQ: $300M: Build on existing Effective Health Care program
  - NIH: $400M (appropriated to AHRQ, transferred to NIH)
    *RC1- Challenge grants*
    *RC2- Grand Opportunities grants*
  - Office of the Secretary: $400M (allocated at discretion)
  - The Federal Coordinating Council for CER created to offer guidance and coordination on the use of funds
  - Funds are available through 9/30/2010
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CER at AHRQ

• Effective Health Care Program (EHP)
  – Authorized by Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003
  – Formal AHRQ program created in 2005

• Legislation mandated AHRQ is to conduct and support research on:
  – “the outcomes, comparative clinical effectiveness, and appropriateness of health care items and services (including prescription drugs)”
  – EHP focus has been to provide patients, clinicians and policy-makers with reliable, evidence-based healthcare information
Improving Quality and Safety Risks

• EHP uses CER to impact physician-patient decisions based on these principles:
  – **Relevancy**: is focused on actual clinical decisions
  – **Timeliness**: is fast and up-to-date
  – **Transparency**: process involves public nomination and ongoing public comment
  – **Objectivity**: employs methods and scientific rigor in systematic reviews to ensure accurate and unbiased reports
  – **Impact** on priority populations and conditions
Priority Conditions for the Effective Health Care Program

1. Arthritis and non-traumatic joint disorders
2. Cancer
3. Cardiovascular disease, including stroke and hypertension
4. Dementia, including Alzheimer’s Disease
5. Depression and other mental health disorders
6. Developmental delays, ADHD and autism
7. Diabetes mellitus
8. Functional limitations and disability
9. Infectious diseases including HIV/AIDS
10. Obesity
11. Peptic ulcer disease and dyspepsia
12. Pregnancy including preterm birth
13. Pulmonary disease/asthma
14. Substance abuse
Who Conducts the Research?

• Coordinated by AHRQ personnel
• Contracts with multiple independent partners:
  • Stakeholder Group
  • Scientific Resource Center (at OHSC)
  • Evidence-based Practice Centers (EPCs) – 15 national centers
  • Developing Evidence to Inform Decisions about Effectiveness Centers (DEcIDEs) – 13 national centers
  • Centers for Education & Research on Therapeutics (CERTs) – 14 national centers
  • John M. Eisenberg Clinical Decisions and Communications Science Center - (transitioning from OHSC to Baylor)
AHRQ
Effective Health Care Program

Evidence Synthesis (EPCs)
- Systematically reviewing, synthesizing, comparing existing evidence on treatment effectiveness
- Identifying relevant knowledge gaps

Evidence Generation (DEcIDE & CERTs Networks)
- Developing new scientific knowledge to address knowledge gaps
- Accelerating practical studies

Evidence Communication/Translation (John M. Eisenberg Clinical Decisions & Communications Science Center)
- Communicating scientific information in plain language to policymakers, patients, and providers
The John M. Eisenberg Center for Clinical Decisions and Communications Sciences

• Data synthesis results in the production of comparative effectiveness reviews
• The Eisenberg Center uses reviews to construct key messages that are disseminated into products tailored for three populations:
  • a. Providers
  • b. Patients
  • c. Policy-makers
The Research Process

- Nominate & Select Research Topics
- Synthesize & Generate Evidence
- Translate into User Guides
Engage Stakeholders in Topic Selection for the EHC Program

- General Public
- Generalist Program Partners
- Key Stakeholder Groups
  - Clinicians
  - Consumers/patients, including consumer/patient organizations
  - Employers and business groups
  - Federal and state partners
  - Healthcare industry representatives
  - Payers, Health Plans, Policy-makers
  - Researchers

Topic Nominations

TOPIC TRIAGE GROUP

Topics selected for further refinement and prioritization

Convened EHC Program Stakeholder Panel and Program Priorities Work Group
EHC Process – Initial
EHC Process – Evolving
How Products Are Used

- Inform clinical guideline development
- Identify future research priorities
- Inform policy, including coverage decisions
- Inform clinician and patient decisions
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Roles for the Implementation Research Community

- Obligation to build on dissemination
- Implementation community can redefine dissemination function
- Innovative opportunities to narrow translation gap
Implementation of key messages

• Passive recipient of CER key dissemination messages

• Traditional implementation role
  – VA QUERI Steps 4, 5, 6

• Obligation for implementation community
  – Dissemination is not adequate
  – Implementation science is necessary to ensure uptake of effectiveness data
Redefining Dissemination

• Actively make transition from dissemination to implementation seamless

• Work actively with dissemination leaders, e.g., Eisenberg Center
  – Potential roles
    • Design and evaluation of dissemination products
    • Shape development of key messages
EHC Process – Initial
“From a Science of Dissemination to Science of Implementation”

Margarita Alegria HSR. 44:5-14.

• Bring implementation variables into key message framing
  – Contextual and local variables
  – Measurement models
• Earlier consideration of implementation
  – Be a part of the discussion
    • Key concept development
    • Key clinical question development
  – Mirrors evolution of Eisenberg Center
EHC Process – Evolving
Translation Barriers

Figure 1. The 2 Translational Blocks in the Clinical Research Continuum

Translation Barriers
- Lack of Willing Participants
- Career Disincentives
- Regulatory Burden
- Practice Limitations
- Fragmented Infrastructure
- High Research Costs
- Incompatible Databases
- Lack of Funding
- Lack of Qualified Investigators

1. Basic Biomedical Research
2. Translation From Basic Science to Human Studies
3. Clinical Science and Knowledge
4. Translation of New Knowledge into Clinical Practice and Health Decision Making

Improved Health

Sung et al. JAMA. 2003, 289(10)
Figure. "Blue Highways" on the NIH Roadmap

Translation Highway

Westfall et al. JAMA. 2007, 297(44)
Translation Time Lag

• 17 year lag from first publication to highly cited clinical trial
  Contopoulos-Ioannidis et al. Science 321:1298-99

• B-Blockers in MI
  – 16 year lag 1980 - 1996 between BHAT trial and designation as quality measure
    – In 1996, only 62.5%
    – In 2005, over 90%

Lee TH. NEJM. 357(12)
Linear Approach to Translation

• T1 → T2
  – 17 years for undisputed clinical trials
• T2 → T3
  – 10 years for widespread guideline implementation
• Does the linear approach to translation contribute to the excessive lag in implementation?
Novel Opportunities

• Implementation Research Community can use novel (non-linear) approaches
  – Integrate Implementation variables into CE reports (synthesis)
  – Include Implementation outcomes as analytic components of CER (generation)
AHRQ
Effective Health Care Program

**Evidence Synthesis (EPCs)**
- Systematically reviewing, synthesizing, comparing existing evidence on treatment effectiveness
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Implementation and Comparative Effectiveness Reviews

- Include implementation variables within CE reviews
  - Contextual factors, geographic and subgroup variance, measures of reach/penetration

- Incorporate these variables as part of the cost-benefit calculations
  - This could actually change key dissemination messages
Implementation and CE Research

• Integrate Implementation into CER studies
  – Understand how implementation variables can change the analysis of CER results
    (Berwick JAMA 2008: Rapid Response Teams)
    • Barriers to intervention uptake, adoption
    • Unexpected outcome event rates
  – Include implementation process and outcome measures as comparative effectiveness outcomes during CER generation
Implementation Should Redefine Comparative Effectiveness

• Efficacy is the measurement of validity in highly controlled settings

• Effectiveness is the measurement of validity in the real-world
  – Implementation should be the bridge
  – Implementation science should establish the bounds for comparative effectiveness
  – Constant feedback between CER and observations of implementation effects
Recasting Translation Pathway

**The Three Translations Required to Improve the Quality of Primary Percutaneous Coronary Intervention (PCI) in Patients with Acute Myocardial Infarction.**

<table>
<thead>
<tr>
<th>Translational Tier</th>
<th>Type of Research</th>
<th>Products of Research</th>
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</thead>
<tbody>
<tr>
<td>T1</td>
<td>Clinical efficacy research</td>
<td>Proof that primary PCI is more effective than fibrinolytic therapy in controlled clinical trials</td>
</tr>
<tr>
<td>T2</td>
<td>Comparative-effectiveness and health services research</td>
<td>Establishment of a 90-minute standard for the interval between arrival in the emergency department and the initiation of coronary intervention</td>
</tr>
<tr>
<td>T3</td>
<td>Implementation research</td>
<td>Identification of hospital-based strategies to reduce the time to PCI and establishment of consortium to guide local integration of strategies</td>
</tr>
</tbody>
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- Not really an example of linear translation
  - Identification “door-to-balloon time” was an implementation outcome
  - Implementation scientists identified process measures to enhance this outcome
  - Continuous cycles of efficacy & implementation

Naik and Petersen. NEJM 2009
For Further Discussion

1) Integrating implementation within the CER dissemination products

2) Incorporating implementation outcomes in reviews of comparative effectiveness

3) Making implementation variables a part of comparative effectiveness studies
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Comments & Questions