

Overview of Comparative Effectiveness Research




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Presentation outline

- **Comparative Effectiveness Research (CER)**
 - **Definitions**
 - Examples
- Patient-Centered Outcomes Research (PCOR)
 - Definitions
 - Examples
- Research methods for CER and PCOR
- CER funding and dissemination



IMPROVING QUALITY
and VALUE in the U.S.
Health Care System
August 2008

Investment in CER holds promise for improving the value of health care over the longer term. Contrary to some common definitions of CER that focus narrowly on supporting and disseminating more head-to-head trials for particular treatments, CER could have a much larger impact if it is more broadly focused on (1) comparing the risks, benefits, and costs of different health care practice; (2) evaluating and revising policies that influence practices; and (3) developing strategies for targeting practices to specific groups of patients. This more broadly conceived approach to CER can support continuing improvements in the delivery system and reduce disparities in health care based on race, geography, and other factors.

Bipartisan Policy Center Leaders' Project, public policy advocacy organization founded by former U.S. Senate Majority Leaders Howard Baker, Tom Daschle, Bob Dole, and George Mitchell

Obama's Budget Increases Funding for Medical Research that Compares Treatment Options

Kaiser Health News, Feb. 1, 2010

The administration, releasing its 2011 budget request to Congress on Monday, proposed spending \$286 million on comparative effectiveness research overseen by the Agency for Healthcare Research and Quality. The agency got \$21 million for such research in its current fiscal-year budget, and an additional \$300 million for such research in the economic stimulus bill.

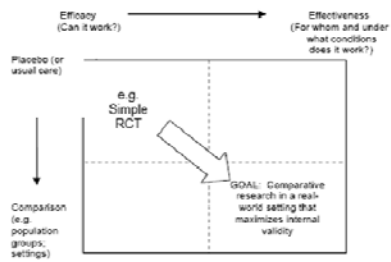
Proponents say the research can provide patients and their doctors with crucial information to help them decide among various drugs or treatments. Critics, on the other hand, say the research could be used to limit or ration care if the federal government or insurers used the information to deny coverage for a particular test or procedure because it was found to be less effective.

Comparative effectiveness research (AHRQ Effective Health Care program)

- Comparative effectiveness research (CER) is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings.
- The purpose is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.
- More simply, what works, for whom, under what circumstances?

Definition of CER

- *Comparison* of two or more health care services or treatments used for a specific disease or condition
- In terms of *effectiveness*, i.e. in approximate real world settings, of the risks and benefits



Comparative effectiveness research

- There are two ways that this evidence is found
 - Researchers conduct studies that generate **new** evidence of effectiveness or comparative effectiveness of a test, treatment, procedure, or health-care service
 - Researchers look at all of the available evidence about the benefits and harms of each choice for different groups of people from **existing** clinical trials, clinical studies, and other research. These are called research reviews, because they are systematic reviews of existing evidence

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Example: Comparative effectiveness of Lexapro vs. generic SSRIs

- Research questions
 - Consistent with rapid onset of action hypothesis, is initiating treatment of new episodes of depression on Lexapro vs. generic SSRIs associated with
 - lower health care costs
 - clinically meaningful improvements in outcomes
- Studies
 - Retrospective analysis of claims data
 - Treatment persistence
 - Costs
 - Record review

} Propensity score analysis

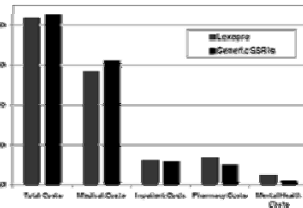
Findings

Treatment persistence

- Consistent with the rapid onset of action hypothesis, patients who initiated treatment with Lexapro were
 - more likely to continue
 - less likely to switch or augment treatment
- Patients discontinuing Lexapro have fewer symptoms in their charts at a follow up visit (*based on 457 charts reviewed*)
 - suggests success rather than failure of treatment

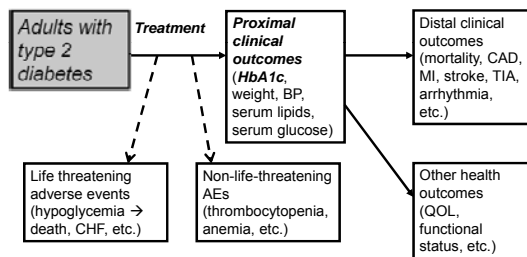
Costs

- Higher drug costs of Lexapro initiators
 - (\$587 vs. \$503, $p < 0.01$)
- more than offset by lower medical costs
 - (\$1,666 vs. \$1,807, $p < 0.01$)
- Total health care costs of Lexapro initiators were lower in the 6 months after initiation
 - (\$2,327 vs. \$2,383, $p < 0.05$)



Example: Comparative effectiveness of oral diabetes medications

- Oral diabetes medication evidence model
 - Setting: Treatment of adults with type 2 diabetes
- Study questions
 - Do medications *differ* in their ability to affect proximal clinical outcomes: HbA1c, weight, blood pressure, ...



Effectiveness of oral diabetes medications: HbA1c

Appendix Table 1. Summary Measures: Weighted Mean Absolute Difference in Hemoglobin A_{1c} Level between Groups for Randomized, Controlled Trials Comparing Oral Diabetes Medications with Placebo or Diet

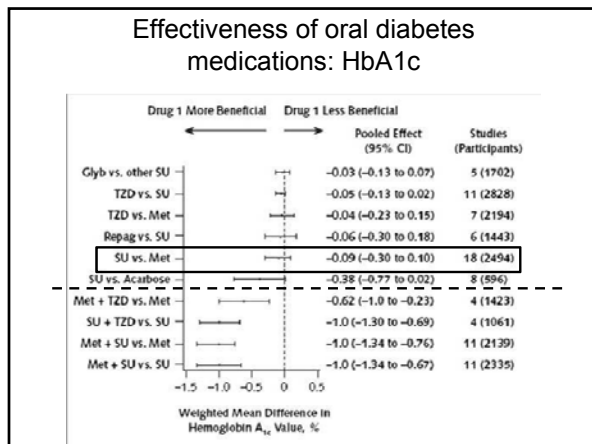
Comparison*	Studies with Data on Mean Differences, n	Weighted Mean Absolute Difference in Hemoglobin A _{1c} Level between Groups (95% CI), %
Pioglitazone vs. control	9	-0.37 (-1.16 to -0.79)
Rosiglitazone vs. control	8	-1.16 (-1.39 to -0.92)
Metformin vs. control	15	-1.14 (-1.4 to -0.87)
Sulfonylureas vs. control	11	-1.52 (-1.75 to -1.28)
Repaglinide vs. control	4	-1.32 (-1.9 to -0.8)
Nateglinide vs. control	4	-0.54 (-0.8 to -0.27)
Acarbose vs. control	28	-0.77 (-0.9 to -0.64)

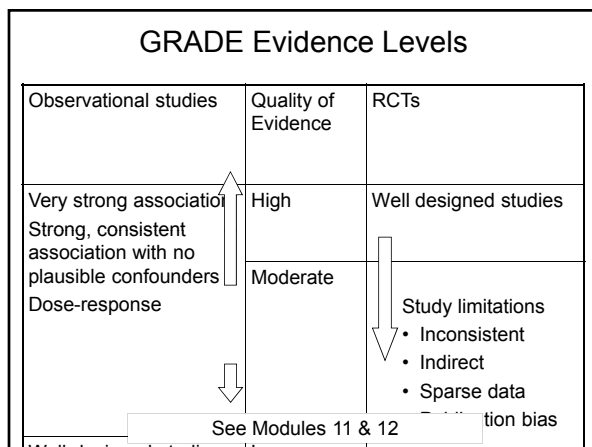
* The control group consisted of placebo or diet.

Indirect comparisons:

Metformin vs. sulfonylureas: $(-1.14) - (-1.52) = 0.38$ (95% CI: 0.03, 0.73)

CI based on pooled variance from placebo meta-analysis w/ $s^2_{\Delta} = s^2_1 + s^2_2$





- ### HbA1c conclusions
- Most oral diabetes medications as monotherapy had similar reductions in HbA1c
 - ~1% absolute reduction
 - direct RCT data; level of evidence “moderate to high”
 - No evidence that particular monotherapies are more effective than others
 - Combination therapies had an additive effect and were better at reducing HbA1c than monotherapies
 - ~1% absolute reduction
 - head-to-head trials; level of evidence “moderate to high”

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Politics of CER

- “As we move forward with comparative effectiveness and evidence-based medicine, we need as much data as possible.”
- We should create “a comparative effectiveness institute” that would use a national, electronic health information system to “collect and understand the best practices of the country’s best providers of care.”
- This institute “could not only educate other providers on how to improve, but also inform policy makers on how to design policy that promotes these best practices.”
 - ??? Newt Gingrich, 2008
- “In our country, the road to dehumanizing, bureaucratic health care rationing begins with something called comparative effectiveness research.”
 - ??? Newt Gingrich, 2010

PCORI

- Affordable Care Act → Patient-Centered Outcomes Research Institute
 - Not “CER” -- tainted as “rationing”
 - Reflects interest in patient-centered care
- Purpose: “to assist patients, clinicians, purchasers, and policy makers in making informed health decisions”
- Public-private organization to disburse federal funding for CER (billions of \$\$)
 - 21 member board of governors (AHRQ, NIH)
 - Methodology committee: “standards”

Patient-Centered Outcomes Research (PCOR) <http://www.pcori.org/>

- PCOR helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of options
- PCOR answers patient-centered questions such as
 - 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 they work in help me make the best decisions about my health and healthcare?

CER vs. PCOR

- Both responsive to specific “priority” clinical topics and populations
 - AHRQ priority populations and conditions
 - IOM CER priority projects
- PCOR aspires to give voice to the patient while helping patients improve their experience and decision making in the healthcare system
 - not all research that might help a patient make decisions or improve their experience in the healthcare system is comparative
 - comparative evaluations do not necessarily incorporate the patient’s voice, outcomes that matter to patients or comparisons that they value

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PCORI priorities

- Based on statutory requirements, working definition of PCOR, and previous research prioritization efforts
 - Assessment of prevention, diagnosis, and treatment options – projects that address critical decisions that patients, their caregivers and clinicians face
 - Improving healthcare systems – projects that address critical decisions that face health care systems, the patients and caregivers who rely on them, and the clinicians who work within them
 - Communication and dissemination research – projects that address critical elements in communication and dissemination among patients, caregivers and clinicians
 - Addressing disparities
 - PCOR methodological research

Sample PCOR questions

Assessment of prevention, diagnosis, and treatment options – critical decisions that patients, their caregivers, and clinicians face

- A 48-year-old woman has recently completed radiation for a small growth in her breast. Her doctors currently see no signs of disease but recommend that she continue to be monitored for potential recurrence. What is her optimal management strategy?
- A 50-year-old woman is diagnosed with Parkinson's disease. Given her personal characteristics, what is the comparative effectiveness and harms of the strategies available to her, especially with regard to cognitive and physical functioning?

Sample PCOR questions

Improving healthcare systems – critical decisions that face health care systems, the patients and caregivers who rely on them, and the clinicians who work within them

- An 84-year-old woman with several chronic diseases is having increasing difficulties managing at home alone, but does not want to leave her home or neighborhood for a nursing home. What are the benefits and drawbacks of different programs or services that might help her stay at home and remain independent safely?
- An elderly man has been hospitalized four times in the past year for congestive heart failure. One challenge seems to be related to delays and poor communication during the transition from the hospital back to the primary care doctor. What could the hospital do to help this man reduce his chances of being hospitalized again?

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Alternatives to RCTs for CER

- RCTs provide best evidence of effectiveness
 - but are limited
 - in when and where they can be used
 - by restrictions on subjects to obtain homogeneity
 - by sample size & ability to detect adverse effects
- Electronic clinical and health plan data
 - Large numbers “under observation”
 - Data already in electronic form → low cost
 - Relatively complete information in EMR
 - Reporting bias minimized
- Weaknesses
 - Possibility (likelihood?) of selection bias
 - Incomplete information on confounders
 - Data quality issues
- How do we balance the
 - rigor and internal validity of RCTs
 - relevance and external validity of observational studies

Controlling bias (threats to validity) through study design and analysis

- Select data sources, patient populations, inclusion/exclusion criteria, and comparators for which bias is likely to be minimal
- Pragmatic trials (Modules 15 & 16)
- Adjust for bias and confounding through
 - multivariate regression (Module 1)
 - propensity score weights or matching (Modules 3&4)
 - instrumental variables (Module 5)
- Use appropriate study designs
 - cohort, case-control etc. (Module 2)
 - AHRQ: Developing a Protocol for Observational Comparative Effectiveness Research
<http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1166&ECem=130212>

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CER funding and resources

- Patient-Centered Outcomes Research Institute (PCORI) (<http://www.pcori.org/>)
- Agency for Healthcare Research and Quality (AHRQ) Effective Health Care program (<http://effectivehealthcare.ahrq.gov/>)
 - Evidence-based Practice Centers (EPCs)
 - DECIDE (Developing Evidence to Inform Decisions about Effectiveness) Network
- NIH National Center for Advancing Translational Sciences “T3” (<http://www.ncats.nih.gov/>)
- Industry
- “Delivery system science”

CER educational and training resources

- OSU Center for Health Outcomes, Policy, and Evaluation Studies (<http://www.cph.osu.edu/hopes/cer>)
- AcademyHealth
 - Health Services Research (HSR) Methods (<http://www.hsrmethode.org/>)
 - Electronic Data Methods (EDM) Forum (<http://www.edm-forum.org>)
 - eGEMs (Generating Evidence & Methods to improve patient outcomes) (<http://repository.academyhealth.org/egems/>)
- AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Reviews
 - (<http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=318>)
- PCORI Methodology Committee
 - (<http://www.pcori.org/research-we-support/methodology/>)
