Institute of Medicine
Committee to set Priorities for Comparative Effectiveness Research

Harold C. Sox, M.D., MACP
(committee co-chair)
Editor, Annals of Internal Medicine

Disclaimer

- **Everything I will say is in the public domain.**

CER

- Comparative
- Effectiveness
- Research

The Promise of CER

Information to help doctors and patients make better decisions

CER in the American Recovery and Reinvestment Act of 2009

- **$1.1B for CER research**
  - $400M to NIH
  - $300M to AHRQ
  - $400M to the Secretary, DHHS
- **Funding timeline**
  - Must obligate the money by the end of 2010

The Committee's working definition of CER

- "The generation and synthesis of evidence that compares the effectiveness of alternative methods to prevent, diagnose, treat, monitor, and improve delivery of care for a clinical condition.
- The purpose of CER is to assist patients, clinicians, purchasers, and policy makers in making informed health decisions."

Source: iom.edu/cerpriorities

What's unique about CER?
It includes all of the following

- Direct, head-to-head comparisons.
- Study populations representative of clinical practice
- Patient-centered
  - tailor the test or treatment to the specific characteristics of the patient.
- Broad range of topics.
  - tests, treatments, strategies for prevention, care delivery and monitoring
- a broad range of beneficiaries:
  - patients, clinicians, purchasers, and policy makers.

“Patient-centered”

- **Suppose a RCT shows that A>B, but many patients got better on B.**
  - **Lacking any additional knowledge, you should prefer A.**
- **Is it possible that some patients would have done better on B than A?**
  - **Can we identify them in advance?**

An example:
CER applied to genetic testing for diabetes susceptibility

An example of CER to inform decision making about genetic testing

- **Background:**
  - Genome-wide association studies have identified several loci associated with Type 2 diabetes.
- **Purpose:**
  - To examine joint effects of genetic loci and conventional DM risk factors.
  - "Do genetic loci add usefully to predicting who will develop diabetes?"

Conventional and genetic risk factors for diabetes

- **Predict onset of DM in**
  - the Nurses Health Study cohort (N=121K women)
  - The Health Professionals Follow-up Study (N=51.5K men)
- **Case-control study**
  - Cases: developed diabetes
  - Matched controls: did not develop DM
  - Exposure: genetic loci and conventional risk factors

Conventional and genetic risk factors for diabetes

- **Case-control study**
  - Cases: developed diabetes
  - Matched controls: did not develop DM
  - Exposure: genetic loci and conventional risk factors
- **Analysis**
  - Calculate OR for exposure (case vs. control)
  - This is equivalent to OR for being a case given exposure vs. no exposure.

Conventional and genetic risk factors for diabetes

- **Conventional risk factors**
  - BMI, physical activity, energy intake
- **Genes**
  - Calculated a genetic risk score (GRS)
  - 17 SNPs
  - Additive model
  - Weighted model
- **Multivariate model to predict DM risk**

Odds ratios for developing DM

	1st Quintile of GRS	2nd Quintile of GRS	3rd Quintile of GRS	4th Quintile of GRS	5th Quintile of GRS
Men	1.0	1.28	1.59	2.09	2.72
Women	1.0	1.01	1.50	1.95	2.02

Adjusted for age, BMI, family history of DM, smoking, menopausal status, alcohol, physical activity.

Measure of discrimination

- **The area under the ROC curve =**
  - **The probability that a person who is destined to develop DM will have a higher score than someone who is not destined to develop DM.**
- **AUC**
  - **Conventional risk factors only: 0.78**
  - **Conventional + GRS: 0.79**

Why does genetic information add so little discriminatory power?

- **Co-linearity:**
  - The genetic factors influence diabetes risk through the conventional risk factors
- **Ceiling effect**
  - 0.78 is very good discrimination; genetic information can't add much.
- **AUC is a poor measure**
  - Reclassification indices may be better

Setting national priorities for CER

The language of the ARRA: about the IOM

- **$1.5M to the IOM to produce a report to Congress and the Secretary by June 30, 2009.**
- **To include recommendations on the national priorities for CER to be conducted or supported with the funds provided (to the Secretary).**
- **Committee must consider input from stakeholders.**

Source: the ARRA of 2009

Stakeholder input

- **March 20th open meeting at NAS building**
  - **56 presenters**
- **Web-based survey open to anyone**
  - **iom.edu/cerpriorities**
  - **Ask for 3 condition-intervention pairs in order of priority**
  - **~1000+ unique respondents**
  - **~2000+ nominations**

Priority-setting criteria

- morbidity and mortality
- variability in care
- cost
- information gap
- funding gap (e.g., minimal research is being done)
- public interest
- controversy
- disproportionate impact on small subpopulation
- potential to act on the information once generated
- utility of the answer for decision-making
- disease burden

Source: iom.edu/cerpriorities

Portfolio Criteria

- **The committee should develop a balanced portfolio of topics for CER research.**
  - **Avoid having all the topics be on heart disease or for adults**
- **What criteria should the committee use to be sure it has a balanced portfolio?**

Next steps

- Report enters National Research Council review process
- Report due June 30, 2009

What will Congress do?

What will Congress do?

- **The Senate Finance Committee white paper:**

Call to Action: Health Reform 2009

Google: Senate Finance Committee white paper

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- Several well-respected panels—including
  - the Institute of Medicine (IOM)
    - Knowing What Works (2008)
  - the Medicare Payment Advisory Commission (MedPAC)
  - the Congressional Budget Office (CBO)—
- have called on Congress to create a national entity charged with conducting this type of research.

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- ….this plan would create a new institute charged with identifying the most pressing gaps in clinical knowledge that prevent the health system from delivering the best outcomes for patients.

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- The Health Care Comparative Effectiveness Research Institute …. would be a private, nonprofit corporation with a Board of Governors appointed from the public and private sectors ….
- The Institute would be created as an independent entity to remove the potential for political influence on the development of national research priorities.

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- The Institute should not just recommend areas of inquiry; it should produce the vital information needed.
- It should be able to contract with experienced Federal agencies, like NIH, and AHRQ….
- The Institute must also have flexibility to meet its priorities by contracting directly with private researchers ….

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- Activities of the Institute should be open to public input and transparent in order to maintain integrity of the research.

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

- Most importantly, the Institute should be subject to rigorous oversight of its finances and mission in order to maintain the public trust.
- These new endeavors would need an adequate and stable source of funding
- … the information produced by such an Institute would benefit all Americans….so it makes sense for a small assessment on private health insurers to be included.

http://finance.senate.gov/healthreform2009/finalwhitepaper.pdf

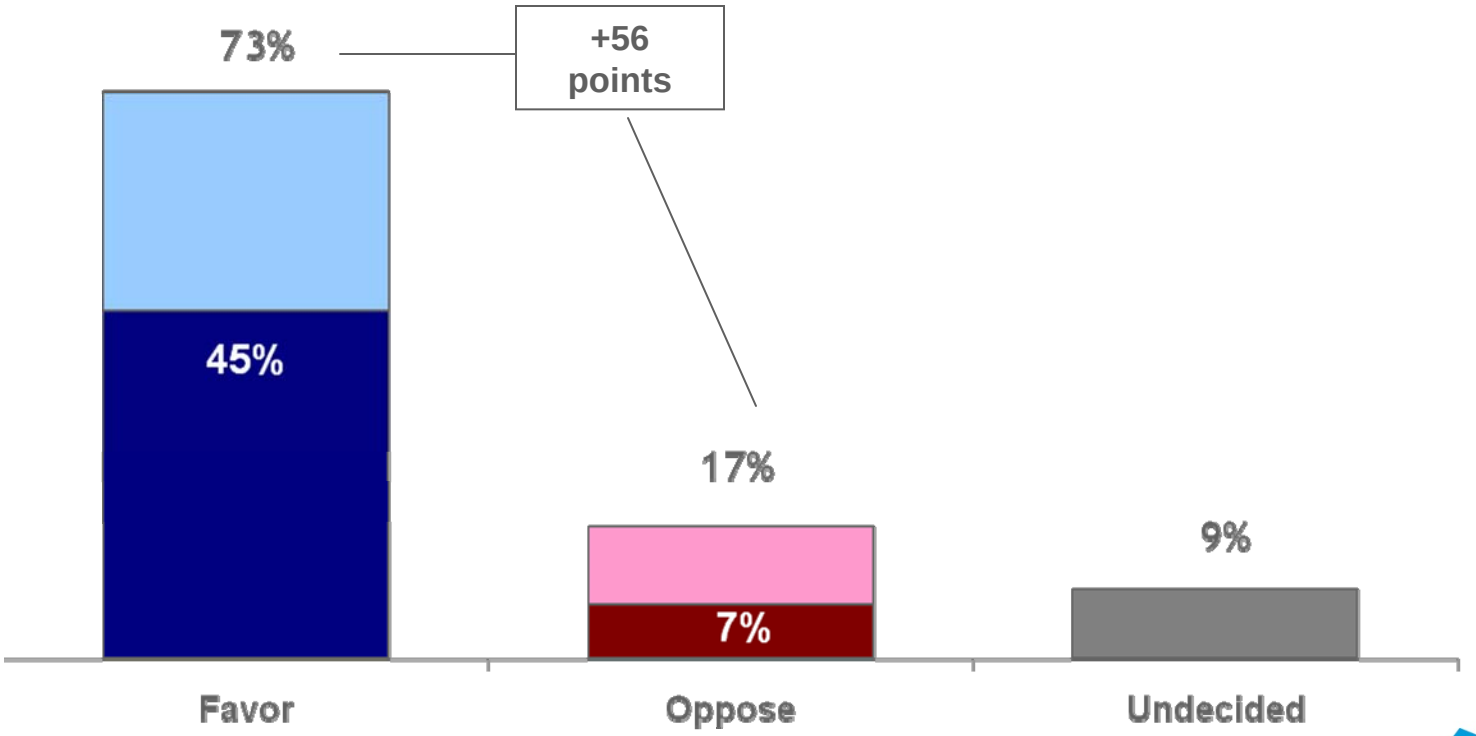
Public attitudes toward CER

Public attitudes toward CER

- **Scott Gottlieb, M.D. (former deputy commission of the FDA):**
  - Negative op-ed in the WSJ
- **Rush Limbaugh**
- **The American Public**
  - National poll commissioned by the Herndon Alliance

Instituting comparative effectiveness reforms to supplement doctors' clinical knowledge has solid support. Voters need to be reassured that scientific and cost effectiveness data do not replace their doctor's judgment.

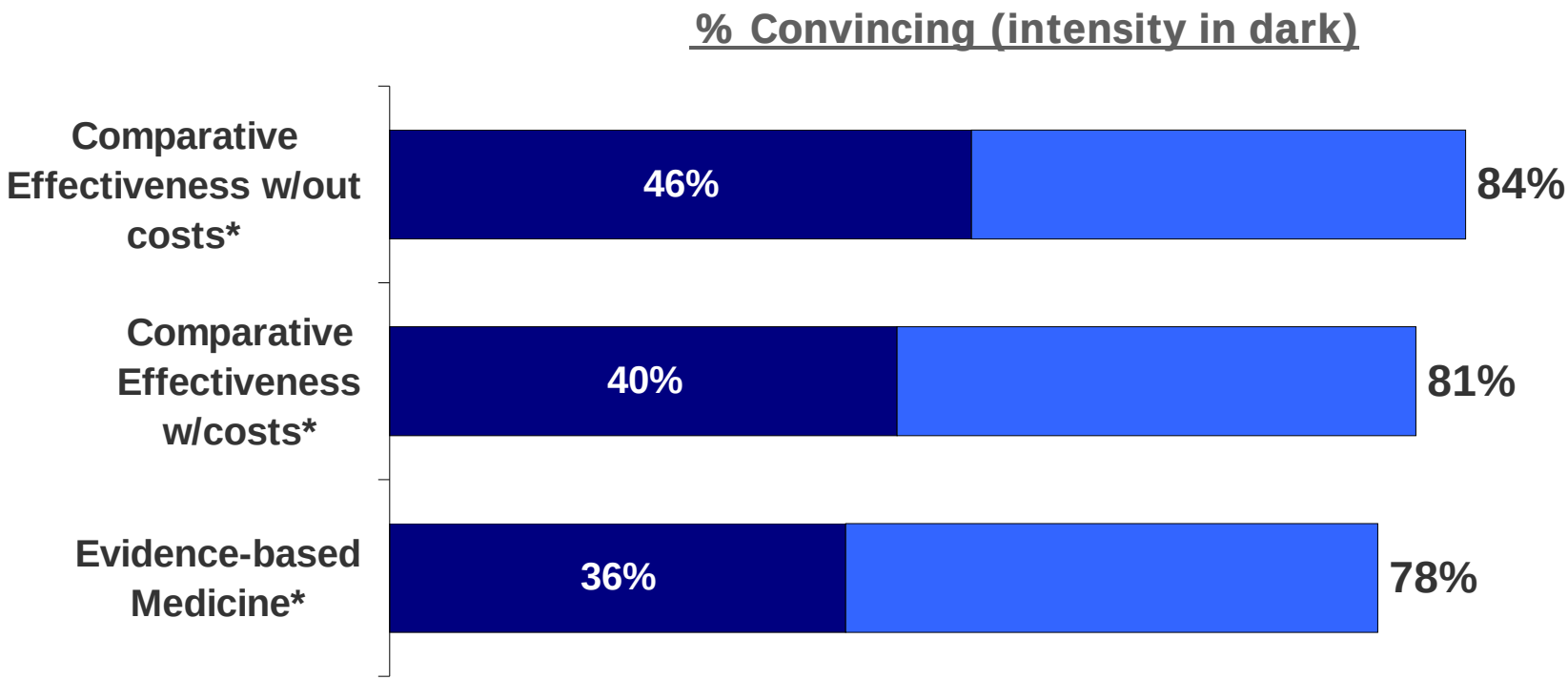
We should create an independent national organization that supports health care providers by giving them information about the most effective treatments. This information would be based on the best available evidence from scientific research and would help ensure that doctors are relying on independent evidence as well as their own personal judgment when making decisions about a patient's care.



* Asked of half of sample.

Messages in favor of reform test very strongly, especially messages that reinforce giving doctors information to provide good care. Comparative effectiveness has overwhelming support with or without explicitly mentioning costs.

Now I am going to read you a series of statements people have made in support of health system changes like those we have been discussing. Please tell me whether each is a very convincing, somewhat convincing, not very convincing or not at all convincing reason to support these changes to the health care system.



* Asked of half of sample.

The Promise of CER

Information to help doctors and patients make better decisions