

Comparative Effectiveness  
Research:  
opportunities for rapid learning  
health care systems

Harold C. Sox, M.D., MACP

Co-chair, the IOM committee  
for initial priority setting for CER

Editor Emeritus  
Annals of Internal Medicine

“Seriously, we basically have to solve the health cost problem, or nothing else matters.”

Paul Krugman

NY Times blog on restoring a healthy  
US economy, September 28, 2009

About fifteen years ago, it seems, something began to change in McAllen. A few leaders of local institutions took profit growth to be a legitimate ethic in the practice of medicine. Not all the doctors accepted this. But they failed to discourage those who did.

Atul Gawande

The Cost Conundrum

The New Yorker, June 1, 2009

Physicians in places like McAllen  
behave differently from others.  
The \$2.4-trillion question is why.  
Unless we figure it out, health  
reform will fail.

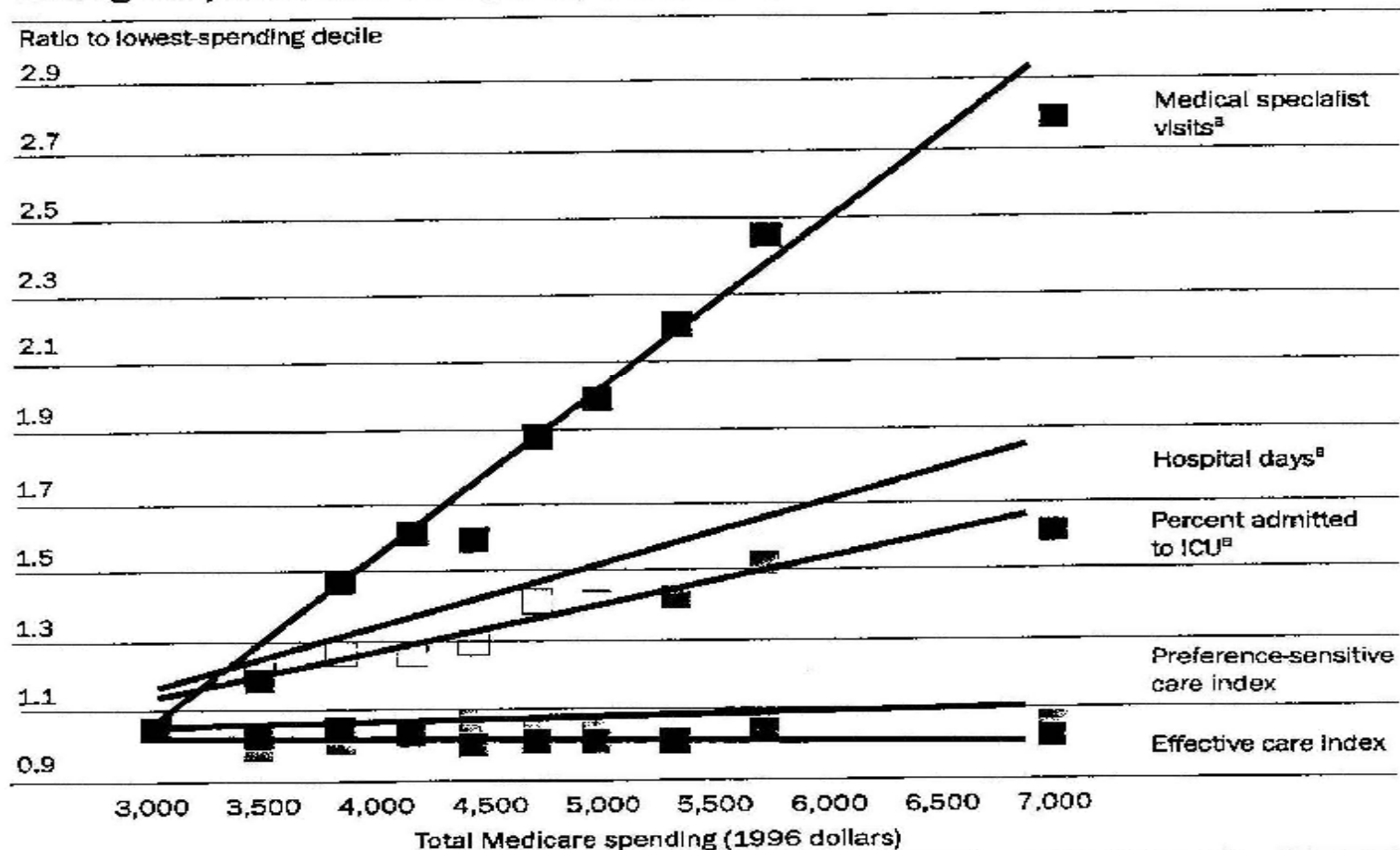
Atul Gawande

The Cost Conundrum

The New Yorker, June 1, 2009

# What expenditures drive small area variations?

**EXHIBIT 2**  
**Use Of Effective Care, Preference-Sensitive Care, And Supply-Sensitive Care**  
**Among Hospital Referral Regions, Grouped By Per Enrollee Spending Level**



# A rationale for CER

- When the evidence is good, service rates don't vary across low and high utilization regions.
  - That should be reassuring.
- When evidence is lacking, rates are higher in regions with high utilization.
- Perhaps—just perhaps—better evidence will reduce unwanted variation in health care practices.

# The IOM Committee's working definition of CER

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.

# What's unique about CER?

It includes all of the following

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

# “Patient-centered”

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

# The Promise of CER

Information to help doctors and patients make better decisions

# IOM Committee's Voting Process

**2,606 recommended CER topics received from 1758 respondents  
to web-based questionnaire**



**Round1 Voting = 1,268 nominated topics → 200 topics**



**Round 2 Voting = 145 rank-ordered topics**



**Committee discusses each topic  
Round 3 Voting on 155 nominated topics**



**Round 3 Results = Final 100  
priority topics**

# Sample top quartile topics

- Compare the effectiveness of dissemination and translation techniques **to facilitate the use of CER** by patients, clinicians, payers, and others.
- Compare the effectiveness of interventions (e.g., community-based multi-level interventions, simple health education, usual care) to **reduce health disparities** in cardiovascular disease, diabetes, **cancer**, musculoskeletal diseases, and birth outcomes.
- Compare the effectiveness of management strategies for ductal carcinoma in situ (**DCIS**).

# Cancer-related top quartile topics

- Compare the effectiveness of **genetic and biomarker testing and usual care** in preventing and treating breast, colorectal, prostate, lung, and ovarian **cancer**, and possibly other clinical conditions for which promising biomarkers exist.
- Compare the effectiveness of **imaging technologies in diagnosing, staging, and monitoring patients with cancer** including positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT).
- Compare the effectiveness of **management strategies for localized prostate cancer** (e.g., active surveillance, radical prostatectomy [conventional, robotic, and laparoscopic], and radiotherapy [conformal, brachytherapy, proton-beam, and intensity-modulated radiotherapy]) on survival, recurrence, side effects, quality of life, and costs.

# The IOM: the CER program should also:

- Do priority-setting on an ongoing basis.
- Have a broadly representative oversight committee
- Engage public participation at all levels of CER
- Support large-scale, clinical and administrative data networks
- Do research on dissemination of CER findings
- Support research and innovation in the methods of CER
- Expand and support the CER workforce

Everyone has an interest in  
seeing CER succeed

What can you do to help?

# Helping CER to succeed

- Make sure that CER funds are used to support CER, with its focus on better decision making, typical study populations, and head-to-head comparisons.
  - Funding agencies, researchers, study sections
  - Public participation can help to hold funding agencies accountable
- Hold authors to high standards of research practice: a role—and a challenge--for journals.

# A journal editor's perspective

- The role of journals
  - Decide which research has enough potential to improve practice to be subject to confirmation by other scientists
  - Transparent, unbiased reporting
  - Evaluate research: a public good
- Requires intense, expensive, sometimes protracted effort that few journals can afford
  - Authors interacting with statisticians and editors
- The result: <10% acceptance rates

# CER methodological challenges to researchers and journals

- Focus on decision making
  - The scope of CER should include research on all aspects of decision making by doctors and patients.
- Less transparent methods:
  - Adaptive trials
  - More complex modeling (systems biology)
- Observational research on huge data sets taken from the records of actual patient care
  - Fast, cheap, and representative but big methodological problems:
    - missing data
    - missing outcomes
    - unmeasured confounders

# CER methodological challenges

- Finding the clinical predictors of response to treatment A and treatment B.
- Trying to measure the value of tests
  - predicting current disease status (sensitivity, specificity, post-test probability)
  - Predicting future outcomes

# CER methodological challenges

- Adherence to all but the simplest guidelines is relatively poor.
- We need to identify interventions that improve adherence to good practice
  - A high priority topic for the IOM committee
  - Study designs often leave doubt about whether the results are correct.

# Questions for the future

- Will Congress enact a national CER program?
- Will the Program promote research that reflects the definition of CER?
- Will the IOM committee's priority list influence funding agencies?
- Will doctors and patients use the results of CER?
- Will learning health care organizations learn to use evidence to inform decisions?
- Will professionalism prevail over profit-taking?

# A question for learning health care systems

- Inferences from observational data are prone to error.
- How should we use the results of *in silico* observational research?
  - With due caution.
- How should we minimize the harms of decision making based on *in silico* research?

# How should we minimize the harms of decision making based on *in silico* research?

- Data quality:
  - data-gathering protocols
  - systematic follow-up
  - ask the reason for choosing a treatment.
- Analysis
  - Build in analytic guidance systems
  - Require basic statistical skills before access to data
  - Independent clinical epidemiology and statistical review before acting on findings.
  - Journal-like function to assure transparent, unbiased reporting.