CER 2010: Critical Overview of the Current Science and Politics of CER

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Overview

- **What is “Comparative Effectiveness Research”?**
- **Why now?**
- **What now?**
- **Three Transformational CER Trial Initiatives**
- **CER in Perspective**

What is “Comparative Effectiveness Research”?

Comparative effectiveness research 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 of this research 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.****

*Federal Coordinating Council for Comparative Effectiveness Research

Does CER Mean “Trials”?

Only in part! CER includes…

- Pragmatic *comparative* clinical trials
- Probably not so pragmatic clinical trials
- Systematic reviews of trials
- Systematic reviews of trials and observational studies
- Simulations and decision-analytic models
- Registry studies
- Data base analyses
- Etc.

Are There Accepted Standards of Evidence for CER Studies?

No!

- Issue needs to be addressed
- Rawlins*: Evidence to be “fit for purpose”
- Slutsky & Clancy (AHRQ): Study designs to be “high quality” & “appropriate” for question
- Gottlieb & Klasmeier**: FDA adopt Federal-wide standard “substantial clinical experience”
- Recent RFP: Evidentiary Standards for CER: Comparison between Regulatory & Non-Regulatory US Government Health Agencies
- Outcomes should be *relevant* to pts, docs, policy decision-makers

***** Harveian Oration: *De testimonio*: on the evidence for decisions about the use of therapeutic interventions, Lancet, 2008

**“Comparative Effectiveness Research: The Need for a Uniform Standard”. AEI, June 2009

At its core….

….CER is a health policy initiative to improve evidence of alternative clinical courses of therapy (or prevention) to inform health care decision making.

So, why now?

Historical Overview: Health Policy Evidence Eras in the US

- 1970s: Health Technology Assessment (HTA)
- 1980s: Effectiveness Research
- 1990s: Outcomes Research
- 2000s: Evidence-Based Medicine
- Of Late: "*Comparative Effectiveness Research*"
- Coming?: "Payment for Outcomes"

Failure of Early Federal Efforts

- Congress's Office of Technology Assessment (1970s-1995)
- National Center for Health Tech Assessment (1978-1981)
- IOM's Council Health Care Technology 1977-1981
- Agency Health Care Policy & Research Clinical Guidelines (Mid-1990s)
- Medicare's Cost-Effectiveness Coverage Rule (1989-present)

Why Did Early Federal Efforts Fail? Were Seen as Threatening to…

- Innovation
- Medical autonomy
- Market access

Thus, these efforts lost political support.

Meanwhile, Private Sector Activities Succeeded in the US

- BCBSA's Technology Evaluation Center
- AMA's Diagnostic and Therapeutic Tech Assessment
- American College of Physicians' Clinical Efficacy Assessment Project
- Academy of Managed Care Pharmacy's Format for Formulary Submissions
- Oregon's Drug Effectiveness Review Project
- Other private sector (e.g., Kaiser, ECRI, Hayes)
- Other public secton (e.g., VA, DoD)

…and continue to succeed

Why Did Private Sector Activities Succeed?

- Perceived as useful by the market
  - Clinical decision making
  - Purchasing
  - Coverage, formulary placement
  - Cost containment
- Politically insulated

Also……

...Many International Public Sector Activities Succeeded

- UK (NICE)
- Australia (PBAC)
- Canada (CADTH)
- Other EU Countries

…because…

…Perceived to be useful in…

- Social equity
- Coverage
- Pricing
- Cost containment
- Value for money spent
- Clinical decision-making

Now, Since Late 1990s in US, Deepening Federal Commitment

- Agency HC Research & Quality (AHRQ)
  - 41 Evidence-related Centers! (Medicare Modernization Act of 2003)
- Medicare
  - Medicare Evidence Development & Coverage Advisory Committee (MedCAC)
  - "Coverage with Evidence Development" Policy
    - » "Conditional Coverage"
- CER "Stimulus funds" ($1.1B) (approximately half goes to CER trials!)
- Health Reform Legislation:
  - CER Institute
  - Medicare Commission (forerunner of US NICE?)

Why Are Recent Federal Evidence Efforts Succeeding?

Feds learned a political lesson! To…

- Develop evidence at arms length from policy use
- **Ex**clude! cost-related analyses
- Sell Medicare's conditional coverage ("Coverage with Evidence Development") policy as a *positive* way to cover new technology

Also….

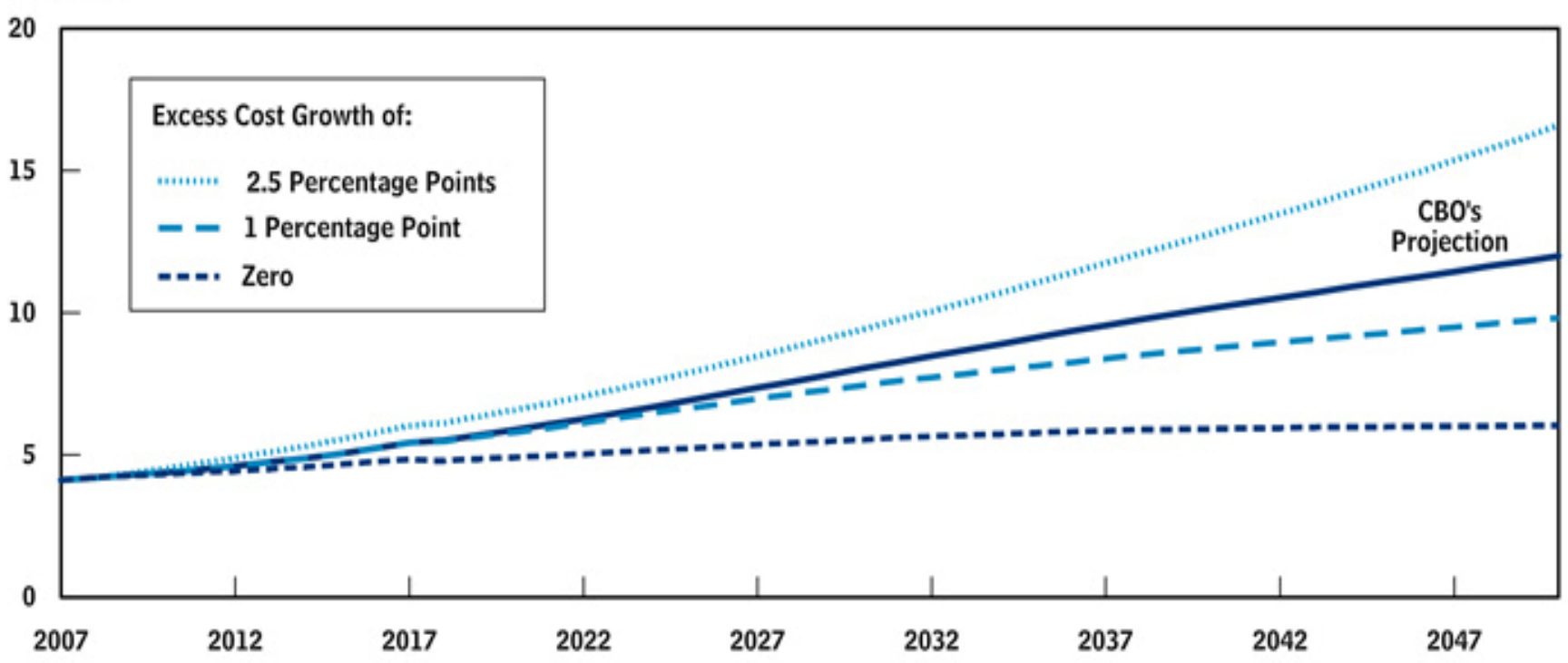
Other Reasons Why Evidence Efforts Are Succeeding

- CER increasingly perceived to be useful and not so threatening
- *Perceived* "Success" of NIH Comparative Trials (e.g., WHI, ALLHAT, CATIE)
- Heightened national concern about cost of health care

Other Reasons (cont.)

- (Erroneous) belief that improving evidence (by itself) will help contain costs
- Belief in a huge evidence gap
- Deepening concern that not getting value for money spent on health care

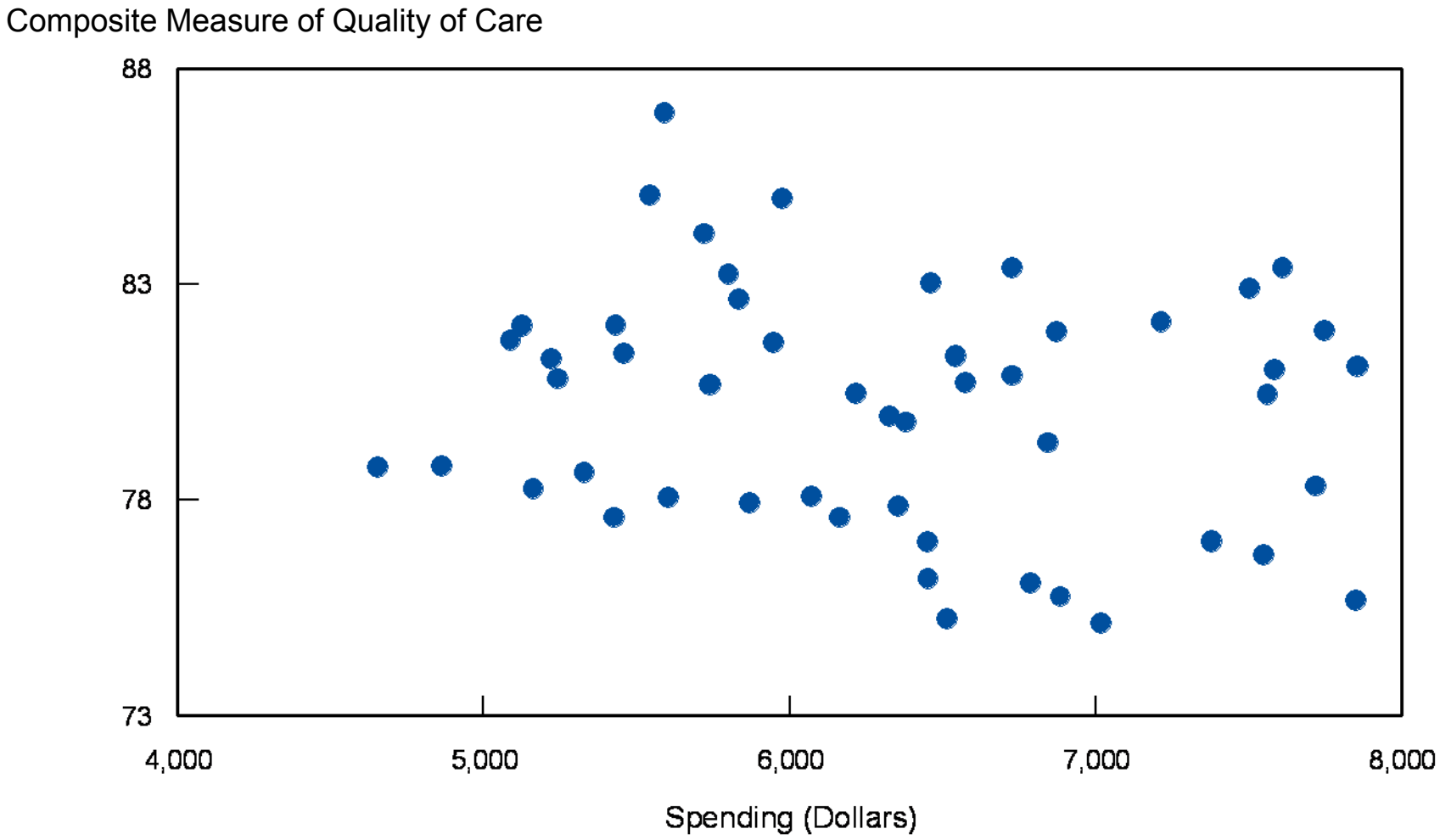
Federal Spending for Medicare and Medicaid as a Percentage of Gross Domestic Product Under Different Assumptions About Excess Cost Growth



Source: Congressional Budget Office.

Note: Excess cost growth refers to the number of percentage points by which the growth of annual health care spending per beneficiary is assumed to exceed the growth of nominal gross domestic product per capita.

The Relationship Between Quality and Medicare Spending, by US State, 2004



Source: Data from AHRQ and CMS (as presented by Dir Orszag, CBO)

Growing National Consensus: Coverage Decisions Should be Evidence-based

"…patients in higher-spending regions received 60% more care… they got more frequent tests and procedures, more visits with specialists, and more frequent admission to hospitals. Yet they did no better than other patients, whether this was measured in terms of survival, their ability to function, or satisfaction with the care they received. If anything, they seem to do worse."

- Atul Gawande, "The Cost Conundrum," The New Yorker, June 1, 2009

What is Happening Now?

Four Major Themes

1. Broad review/overhaul

2. Enhancement of evidence base

3. Conditional coverage; Paying for Outcomes (P4O)

4. Renewed interest in HTA (Health Technology Assessment)

Theme 1:

Broad Review/Overhaul

IOM Roundtable on EBM

- Vision: “Learning Health Care System”
- Goal: By 2030, 90% of all health care decisions be patient-specific, best evidence-based
- Process: Engage all stakeholders, craft an integrated, comprehensive national solution via broad consensus

IOM EBM Roundtable Membership

- CEO, Mayo (Chair)
- CEO, Keas, Inc.
- CEO, AstraZeneca
- **Administrator**, AHRQ
- President, National Business Group on Health
- President, Consumers Union
- President & CEO, Kaiser Permanente
- President, Milbank Memorial Foundation
- Chancellor, Emory University
- Undersecretary for Health, DVA
- Chair, Orthopedic Surgery, UVA
- President & CEO, Stryker
- Senior Fellow, Brookings Institution
- Director, NHLBI
- Director, Center for Transitions in Health, UPenn
- VP, Health Solutions Group, Microsoft
- President, AMA
- President & CMO, HCA, Inc.

IOM EBM Roundtable Membership

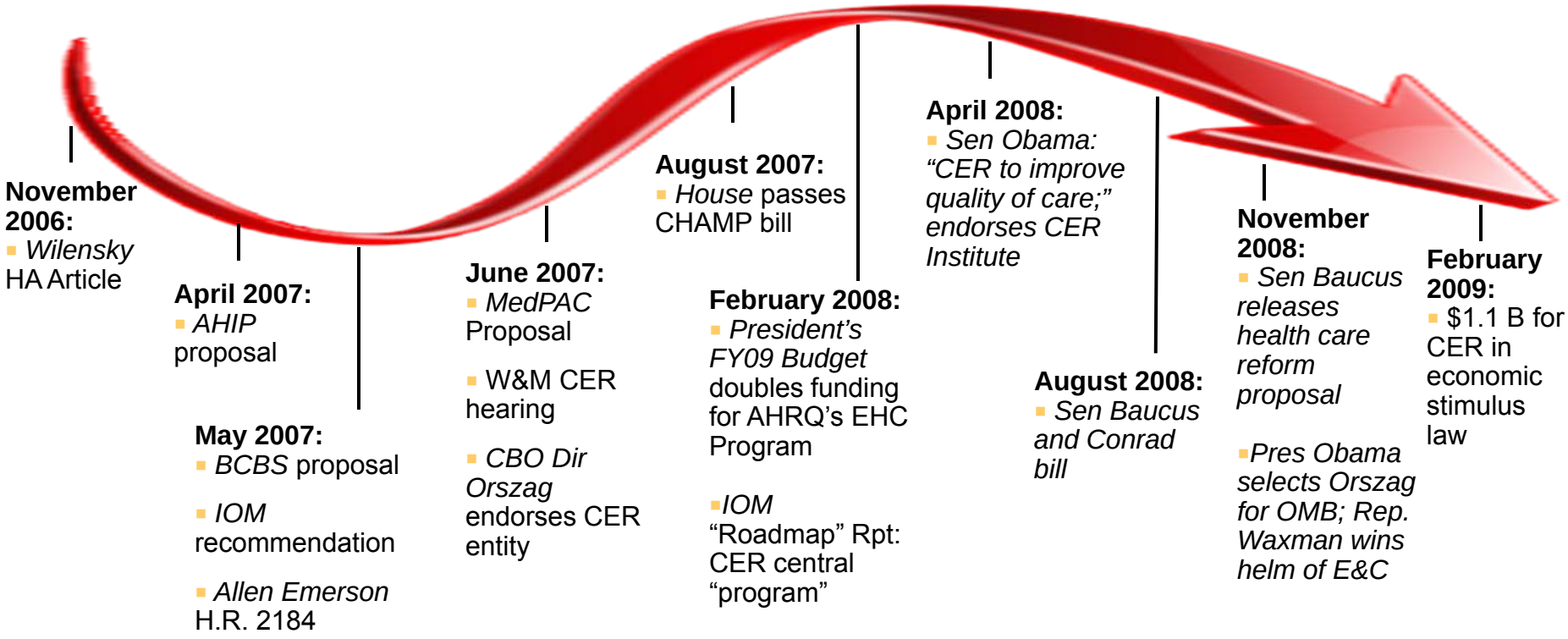
- Professor & Chair, Harvard Medical School & Harvard Pilgrim
- Executive Officer, AARP
- Chairman, sanofi-aventis US
- Former Executive Chairman, Aetna
- Director, HSR, Johns Hopkins
- President, Service Employees International Union
- SVP & CMO, Independence Blue Cross
- President, National Breast Cancer Coalition
- Acting Administrator, CMS
- Chair & CEO, Johnson & Johnson
- Deputy Commissioner & CMO, FDA

Roundtable Workshops & Publications

- "**The Learning Healthcare System"**
- "**Leadership** Commitments to Improve **Value**
- "Finding **Common Ground**"
- "…**Getting Value** Health Care"
- "**Infrastructure** & Clinical Priorities"
- "…**Innovation** & **Practice Based Approaches**"
- "**Clinical Data** as the Basic Staple of Health Learning…"
- **'Rapid learning'** with EMR

Theme 2:
Enhancement of Evidence Base

The *Wave* for Federal Investment in CER



BCBS=Blue Cross and Blue Shield
AHIP=America's Health Insurance Plans
IOM=The Institutes of Medicine

Enhancing the Evidence Base

- Direct federal funding for CER (ARRA: $1.1B)
- Direct federal funding for HIT (ARRA: $20 B)
  - For “Rapid Learning” concept
- Legislation to Create National Institute for CER (Health Reform bills)
  - More funding?

National Institute for CER (Senate bill)

- **"The purpose of the [non-profit] Institute is** *to assist patients, clinicians, purchasers, and policy makers in making informed health decisions by* **advancing the quality and relevance of evidence** *concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed* **through research and evidence syntheses…."**

β *H.R. 3590, Sec. 6301*

Funding for CER Institute*

- US$1.26 billion from General Treasury (total for FY2010-2019)
- Fees on Medicare, insured, and self-insured (FY2013-2019)

* Senate Bill: Patient-Centered Outcomes Research Trust Fund

Theme 3:

Risk Sharing
Conditional Coverage
Pay for Outcomes (P4O)

CMS's Conditional Coverage Policy

Coverage with Evidence Development (CED)

- **Definition:** provides for temporary coverage contingent on the beneficiaries' participation in an organized, payer approved, clinical research program.

- **Purpose:** To generate clinical evidence for coverage decision making.

*Some International Risk-sharing/Value-based Pricing Schemes**

Manufacturer(s)	Drug(s)/Assay	Country (Payer)
Johnson & Johnson	Velcade	United Kingdom (NHS)
Merck	Januvia & Janumet	United States (CIGNA)
Procter & Gamble/ sanofi-aventis	Actonel	United States (Health Alliance Medical Plans)
Novartis	Lucentis	United Kingdom (NHS)
sanofi-aventis	Rimonabant	Sweden (TLV)
biogen idec Schering EMD Serono/Pfizer Teva Phamaceuticals	Avonex Betaferon Rebif Copaxone	United Kingdom (NHS)
Johnson & Johnson	Risperdal Consta	France (HAS)
Genomic Health	Oncotype DX, Breast Cancer Assay	United States (UnitedHealthcare)

*Hunter CA, Glasspool J, Cohen RS, Keskinaslan A. A Literature Review of Risk-sharing Agreements. *Journal of Pharmaceutical Policy Research*, Publication forthcoming.

Theme 4:

Renewed Interest in Health Technology Assessment (HTA)

Renewed Interest in HTA

- Federal Commitment
  - E.g. AHRQ 41 center
- State Commitment
  - E.g. Drug Effectiveness Review Project (14 State Medicaid agencies)
- Private Health Plan Commitment
- Private Manufacture Commitment

Ex of US Private Payer HTA-Related Activity

- WellPoint
  - New HTA Guidelines
  - Willingness to pay for more expensive treatments if “superior clinical CER evidence is available”
- BCBS Technology Evaluation Center (TEC)
  - New drugs must be at least as *comparatively* effective as an established alternative.
- UnitedHealth Care
  - Value-based Insurance Design

Ex of Private Manufacture Commitment

Sponsorship of International HTA Working Group

- **Mission**: "Stimulate discussion of HTA program goals & procedures to enhance HTA rigor, validity & usefulness"
- **Activities**: Published papers, symposia, discussion groups
- **Publications**:
  - 15 HTA Principles. Drummond et al. *IJTAHC,* 24:3 (2008)
  - Do HTA Organizations Use Principles? Neumann et al. *IJTAHC*, 2009
  - Clearing the EBM, HTA, CER Confusion", Luce et al. (in review)

*Unrestricted grant from Merck/S-P

Three Transformational CER Trial-Related Initiatives

Three Transformational CER Trial-Related Initiatives

- Center for Medical Technology & Policy (**CMTP**)
- Clinical Trial Transformation Initiative (**CTTI**)
- **PACE** (Pragmatic Approaches to Comparative Effectiveness) Initiative

Center for Medical Technology Policy (CMTP)

- Provides neutral forums for all stakeholders to work together to design & implement prospective, pragmatic real world clinical studies to inform HC decisions.

- Focuses on methods for evaluating **comparative effectiveness**, including **pragmatic trials**, adaptive designs, clinical registries, and other study designs that generate evidence that will provide patients, clinicians and payers with a reasonable level of confidence in their decision making.

http://www.cmtpnet.org

Ex of CMTP Activities

- **Workshop: “Methodological Guidance for Common Design of Registration & Pragmatic Clinical Trials (5/09, Baltimore)**
- **Purpose:** To develop a conceptual, methodological and policy framework to make registration trials more “pragmatic” and more informative to post-regulatory decision makers.
- **Deliverables:** White paper & Effectiveness Guidance Document (EGD)

Workshop Participants

Academia

Government Clinical Research

Private Payers

Regulators (FDA)

Private Researchers

Public Payer

Patient Representative

HTA Organizations

Manufacturers

Clinical Trials Transformation Initiative (CTTI)

- Public-private partnership (Duke hosts)
- Related to FDA's Critical Path Initiative
- Mission: Clinical trial operational efficiency
  - E.g. Data & AE reporting requirements; IRB simplification, etc.
- Broad membership

*www.**trialstransformation**.org*

CTTI Membership

- Academy of Pharmaceutical Physicians and Investigators
- American College of Cardiology
- American College of Clinical Pharmacology
- American College of Neuropsychopharmacology
- Amgen, Inc.
- Association of Clinical Research Organizations
- bioMerieux, Inc.
- Biotechnology Industry Organization
- Biotronik, Inc.
- Black Hills Clinical Research Center
- Bristol-Myers Squibb Co.
- C.R. Bard, Inc.
- Centers for Medicare and Medicaid Services
- Clinical Data Interchange Standards Consortium (CDISC)
- Daiichi Sankyo Inc.
- Duke University
- Eli Lilly and Company
- Genentech
- GlaxoSmithKline
- Health Decisions
- Hoffman-La Roche, Inc.
- Human Genome Sciences, Inc.
- ICON Clinical Research
- Johns Hopkins University
- Johnson & Johnson Medical Devices & Diagnostics
- Johnson & Johnson Pharmaceutical Research & Development
- King & Spalding LLP
- MedAvante, Inc.
- National Institutes of Health
- Novartis Pharmaceuticals
- Office for Human Research Protections
- Palo Alto Investors, Inc.
- PAREXEL International
- Pfizer
- PharmaNet Development Group, Inc.
- Pharmaceutical Research and Manufacturers of America
- Piedmont Medical Group
- Quintiles
- Rx Trials, Inc.
- Society for Clinical Data Management
- Society for Clinical Trials
- St. Jude Medical
- Target Health, Inc.
- The Medicines Company
- University of California - Davis
- University of Missouri
- University of Oxford
- University of Pennsylvania
- University of Wisconsin
- US Food and Drug Administration
- Wright Medical

The PACE Initiative (Pragmatic Approaches to Comparative Effectiveness)

- Organized by UBC
- Mission: to improve the practicality & analytical efficiency of comparative clinical trials
- Initial focus: Bayesian adaptive methods for CER Trials
- Activities: Scientific & policy forums, sessions, testimony; methods papers, proof of concept; working paper series

www.PACEInitiative.org

Ex of PACE Activities

- National Forum & Publication: "Rethinking Randomized Clinical Trials for Comparative Effectiveness Research: The Need for Transformational Change". *Ann Intern Med.* 2009
- Proof of Concept: "Simulating ALLHAT as a Bayesian Adaptive Trial"
- Working Paper Series:
  - "Thresholds to invest: manufacturers' decisions to sponsor real world comparative trials." A Basu D Meltzer, U of Chic
  - "The use of empirically informative priors in comparative-effectiveness research." D Vanness, U Wisc
  - "Getting to yes: how much additional evidence do payers *really* need to make a coverage decision?" B Luce, UBC

PACE Sponsors & “Collaborating Organizations”

Sponsors & Members

- Amgen, Inc.
- Eli Lilly and Company
- Forest Laboratories, Inc.
- MedImmune, Inc.
- National Pharmaceutical Council
- Boehringer Ingleheim
- Pfizer
- J&J
- Shire
- United BioSource Corporation

Collaborating Organizations

Center for Medical Technology Policy (CMTP)
www.cmtpnet.org

Excellence in Pragmatic and Observational Studies (EXPERT) Global Research Design Network
www.lilly.com

Friends of Cancer Research
www.focr.org

And now….

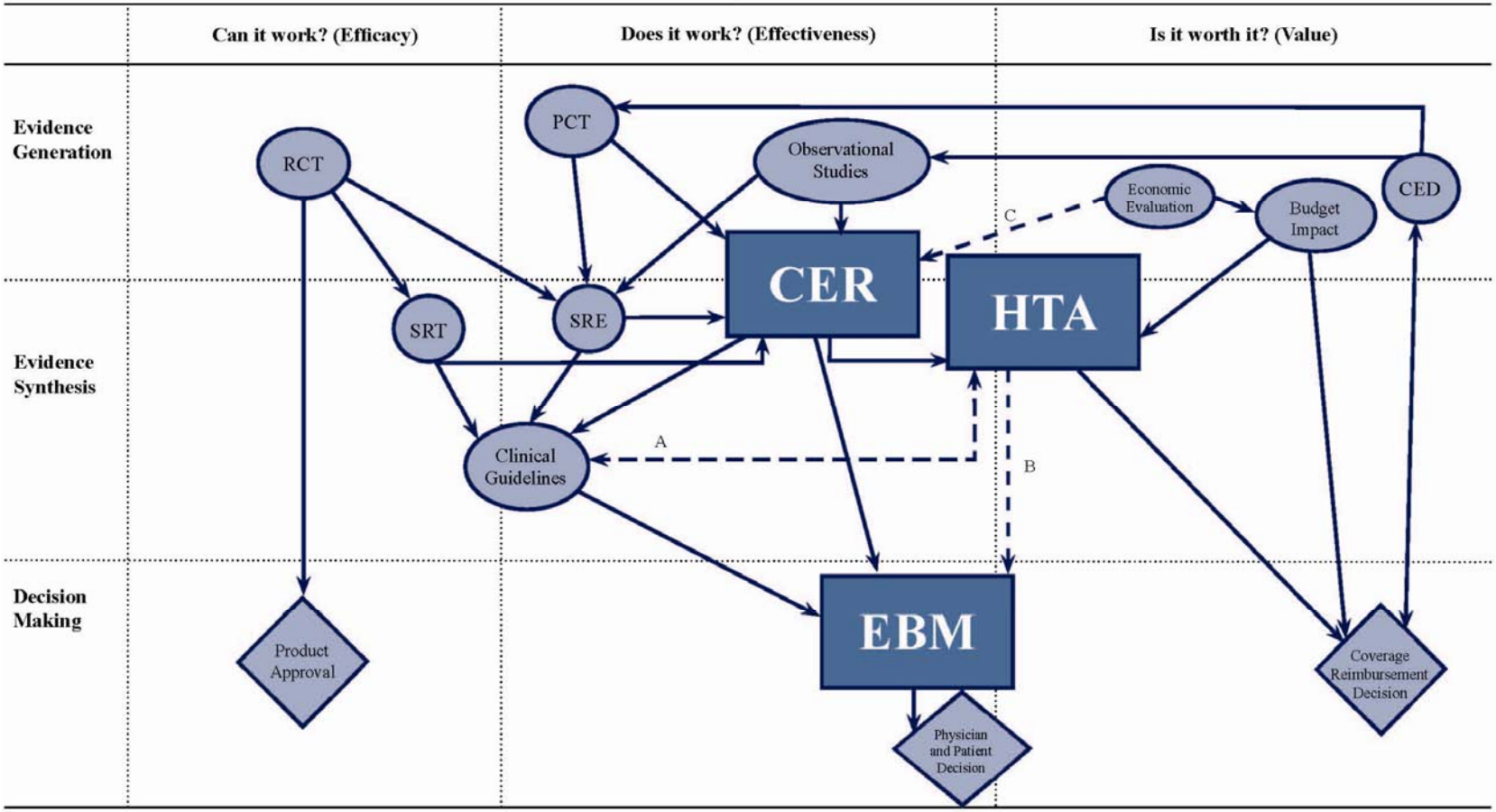
CER

in

Perspective

("If I haven't already confused you enough")

CER in Perspective



RCT = Randomized Controlled Trials; SRT = Systematic Review Trials;
PCT = Pragmatic Clinical Trials; CER = Comparative Effectiveness Research
CEA = Cost-effectiveness Analysis; CED = Coverage with Evidence Development;
EBM = Evidence-based Medicine

In Closing

- CER latest incarnation of a ~ 30 year national evidence policy process
- Public policy interest in CER ~ poor evidence base & exploding costs
- Many aspects about CER still in flux
  - Role of cost analyses
  - Standards of evidence
  - Study types & designs
  - New “transformational” concepts
  - Role in policy formation
  - Role of public vis a vis private sector
  - Stakeholder involvement

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Thank You!