

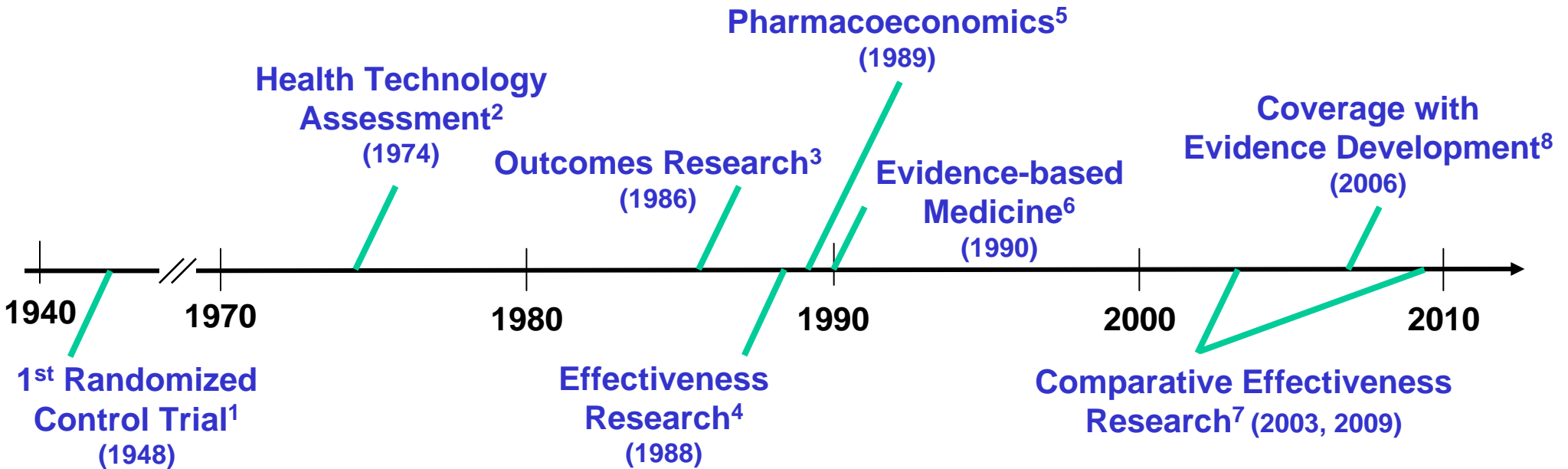
ISPOR 2009

**The CER Train Has Left ... for Where?
Are You on Board?**

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Getting to CER – Inception Timeline



¹ RCT of streptomycin for pulmonary tuberculosis, sponsored by Medical Research Council (UK): 1948

² Origin of TA (not focused on health) in 1965: US Congressman Daddario; first “experimental” HTA by National Academy of Engineering in 1969 (multiphasic screening); Office of Technology Assessment published first HTA in 1974

³ Patient Outcomes Assessment Research Program (later, PORTs) initiated by NCHSR (later renamed AHCPR; now AHRQ) in 1986 (“promote research with respect to patient outcomes of selected medical treatments and surgical procedures for the purpose of assessing their appropriateness, necessity and effectiveness “)

⁴ HCFA (later renamed CMS) Effectiveness Initiative: 1988

⁵ Early published appearance of “pharmacoeconomics”: Bootman et al. 1989

⁶ “Evidence-based”: Eddy 1990; “Evidence-based medicine”: Guyatt et al. 1992

⁷ Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) specifies AHRQ role in “comparative clinical effectiveness”; American Recovery and Reinvestment Act of 2009 (ARRA) authorizes major national investment in CER

⁸ CMS draft guidance in 2005; formalized in 2006. Medicare and other payers began linking coverage to clinical research in 1990s

CER Attributes (1)

No standard definition of CER. Generally common attributes:

- **Direct comparisons of alternative interventions (as opposed to comparison with placebo or indirect comparisons)**
- **May apply to all types of interventions**
 - pharma, biotech, devices/equip't, medical and surgical procedures; organization, delivery, management, financing
- **Effectiveness (in realistic health care settings) rather than efficacy (in ideal circumstances)**
- **Health care outcomes (e.g., morbidity, mortality, QoL, adverse events, and symptoms) rather than surrogates or other intermediate endpoints**

CER Attributes (2)

- **Primary and secondary data collection**
 - **Preferred: head-to-head RCTs/PCTs that meet req'ts for effectiveness research, where feasible**
 - **Observational studies, including registries, claims data, epidemiological; use of EHRs**
 - **Systematic reviews (may include meta-analyses) of head-to-head comparisons (direct preferred over indirect; “comparative effectiveness reviews)**
- **No consensus regarding incorporation of cost-effectiveness analysis or other economic analysis (Back to this later ...)**

CER as Described in ARRA

- ***Provided*, That the funding appropriated in this paragraph shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that:**
 - (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and**
 - (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data ...**

Source: American Recovery and Reinvestment Act of 2009

CER in ARRA

- **Provides \$1.1 B, available through Sept. 30, 2010**
 - **AHRQ: \$300 M**
 - **NIH: \$400 M**
 - **DHHS Secretary: \$400 M**
 - Provide annual report to Congress on CER
 - Provide Operating Plan to Congress for FY 2009 expenditures by July 30, 2009 and Plan for FY 2010 by Nov. 1, 2009
- **Establishes Federal Coordinating Council for CER; allocates \$1.5 M for IOM**
 - **both will advise DHHS Secretary on CER priorities**

Source: American Recovery and Reinvestment Act of 2009

Charge to IOM

- **[P]roduce and submit a report to the Congress and the Secretary by not later than June 30, 2009, that includes recommendations on the national priorities for comparative effectiveness research to be conducted or supported with the funds provided in this paragraph and that considers input from stakeholders.**
- **Report to Congress June 30, 2009**

Source: American Recovery and Reinvestment Act of 2009

Charge to Federal Coordinating Council

- **PURPOSE.**—The Council shall foster optimum **coordination** of comparative effectiveness and related health services research conducted or supported by relevant Federal departments and agencies, with the goal of **reducing duplicative efforts** and **encouraging coordinated and complementary use of resources.**
- **DUTIES.**—The Council shall—
- (1) assist the offices and agencies of the Federal Government, including the Departments of Health and Human Services, Veterans Affairs, and Defense, and other Federal departments or agencies, to **coordinate the conduct or support of comparative effectiveness and related health services research**; and
- (2) advise the President and Congress on—
 - (A) **strategies with respect to the infrastructure needs** of comparative effectiveness research within the Federal Government; and
 - (B) **organizational expenditures** for comparative effectiveness research by relevant Federal departments and agencies.

Source: American Recovery and Reinvestment Act of 2009

Federal Coordinating Council

Agencies represented:

AHRQ

CDC

CMS

DoD

FDA

HHS

- OS

- ASPE

- OD

- OMH

HRSA

NIH

OMB

ONC Health IT

SAMHSA

VA

Initial report due June 30, 2009, on current Federal activities on CER and recommendations for such research conducted or supported under ARRA; annual reports thereafter.

Provisions Distancing CER from Payment Policy

AHRQ: MMA 2003, Section 1013:

- “AHRQ shall not mandate national standards of clinical practice or quality health care standards.”
- “CMS may not use data obtained through this provision to withhold coverage of a prescription drug ... ”

Federal Coordinating Council for CER: ARRA 2009

- “Nothing in this section shall be construed to permit the Council to mandate coverage, reimbursement, or other policies for any public or private payer.”
- “None of the reports submitted under this section or recommendations made by the Council shall be construed as mandates or clinical guidelines for payment, coverage, or treatment.”

Health Reform and CER: Senate Finance Committee – April 29, 2009 (1)

- **ARRA funds are temporary and must be obligated by end of 2010.**
- **Consider options to establish long-term or permanent framework to set national priorities and provide for conducting CER**
 - **Fund existing HHS entities through annual appropriations (as in ARRA)**
 - **Establish private, non-profit Institute for CER**
 - **Balanced, multistakeholder board**
 - **Contract with AHRQ, NIH, other federal and private entities to conduct CER**
 - **Subject to regular GAO reviews**

Source: Description of Policy Options. Transforming the Health Care Delivery System: Proposals to Improve Patient Care and Reduce Health Care Costs. Senate Financing Committee. April 29, 2009.

Health Reform and CER (2)

- **Other optional provisions:**
 - **Expert committee on methodological standards**
 - **Transparency and public input (e.g., via expert advisory panels, public comment)**
 - **Findings understandable to patients and providers**
 - **Account for patient subgroups**
 - **No direct or “fast-track” link to payment**
- **Funding: options**
 - **Annually by appropriations or by mix of public and private sector funds, e.g.:**
 - general revenues, contributions from Medicare trust funds, assessment on private insurance (in proportion to share of total national health expenditures)

Source: Description of Policy Options. Transforming the Health Care Delivery System: Proposals to Improve Patient Care and Reduce Health Care Costs. Senate Financing Committee. April 29, 2009.

Health Reform and CER (3)

No direct or “fast-track” link to payment:

- **Institute or other entity conducting research:**
 - **“should be prohibited from issuing medical practice recommendations or from making reimbursement or coverage decisions or recommendations.”**
- **Medicare could use findings only in way that**
 - **is transparent**
 - **in context of all available evidence**
 - **considers effects on beneficiary subpopulations**
 - **allows public comment on draft proposals that use this information**
- **“This would prohibit HHS agencies from creating a fast-track process for automatically linking research findings to coverage or reimbursement decisions in public programs.”**

Source: Description of Policy Options. Transforming the Health Care Delivery System: Proposals to Improve Patient Care and Reduce Health Care Costs. Senate Financing Committee. April 29, 2009.

Health Reform and CER (4): Just One Element

- **Section I: Payment Reform** – Options to Improve the Quality and Integrity of Medicare Payment Systems
...
- **Section II: Long-Term Payment Reforms** – Options to Foster Care Coordination and Provider Collaborations
...
- **Section III: Health Care Infrastructure Investments** – Tools to Support Delivery System Reform
Health IT
Comparative Effectiveness Research
Transparency
Workforce
- **Section IV: Medicare Advantage** – Options to Promote Quality, Efficiency and Care Management
...
- **Section V: Public Program Integrity**
...

Source: Description of Policy Options. Transforming the Health Care Delivery System: Proposals to Improve Patient Care and Reduce Health Care Costs. Senate Financing Committee. April 29, 2009.

Priority Conditions: AHRQ Effective Health Care Program (arising from MMA Sec. 1013)

- Arthritis and non-traumatic joint disorders
- Cancer
- Cardiovascular disease, including stroke and hypertension
- Dementia, including Alzheimer's disease
- Depression and other mental health disorders
- Developmental delays, ADHD and autism
- Diabetes mellitus
- Functional limitations and disability
- Infectious diseases including HIV/AIDS
- Obesity
- Peptic ulcer disease and dyspepsia
- Pregnancy including pre-term birth
- Pulmonary disease/asthma
- Substance abuse

IOM Committee on CER Priorities, 2009

Priority-setting criteria

- **Disease burden**
- **Increasing prevalence**
- **Morbidity and mortality**
- **Variability in care**
- **Cost**
- **Information gap (e.g., little known about topic)**
- **Funding gap (e.g., minimal research being done)**
- **Public interest**
- **Controversy**
- **Disproportionate impact by subpopulation**
- **Potential to act on the information once generated**
- **Utility of the answer for decision-making**

CER and Personalized Medicine: Contradictory or Complementary?

- **Population-based evidence must be complemented by personalized evidence based on discrete genomic and other personal traits of specific patients**
 - **CER should respond to and support PM**
 - **PM interventions must be supported with evidence of clinical validity and utility from diverse populations and routine health care settings**
 - **Need population-based research with sufficient power for subgroup analyses (esp. prospective) to identify and quantify relationships among genomic traits, biomarkers, therapies and health outcomes**
 - **Integrate research priorities, study design and conduct, reporting, and translation into practice**



The NEW ENGLAND JOURNAL of MEDICINE

Does Comparative-Effectiveness Research Threaten Personalized Medicine?

MAY 7, 2009

Alan M. Garber, M.D., Ph.D., and Sean R. Tunis, M.D.

- ... “The greatest obstacle to the adoption of personalized approaches such as genomic testing, however, is the lack of adequately designed studies assessing their clinical utility.”
- ... “We may know very little about how a test might improve health in typical clinical settings.”
- ... “[O]nce associations between genotype and drug sensitivity have been identified, studies assessing the clinical benefits of gene-guided management strategies will be needed.”
- ... Appropriately designed studies could reveal that a genomic test adds little useful information or, conversely, that the personalized approach works better.

CER – Risky Venture?

Biogen Drug's Steady Return. Wall Street Journal July 21, 2008, B7.

Mr. Mullen [Biogen CEO] said Biogen was planning a “head-to-head” trial of Tysabri to compare its efficacy against a competing MS drug. No such studies have yet been run, meaning nobody knows for sure whether Tysabri is better than competing drugs or by how much....

“That’ll be the next step in the evolution of this product, is running some more directed head-to-head comparators,” Mr. Mullen said. But he cautioned that “the precise trial design has not been agreed upon” between Biogen and [Tysabri marketing partner] Elan and was “probably a few months away.”

Such a study would let doctors better weigh the benefits of different MS drugs....

But it will entail risks. “That certainly wouldn’t be a terribly wise trial,” Mr. Schoenbaum [an analyst at Deutsche Bank who has a “hold” on Biogen’s shares] said. “The vast majority of physicians already believe Tysabri is vastly more efficacious.... On the off chance they lose on a trial like that, they have a lot more to lose than gain.”

CER: Open Questions

- **Continued transparency, stakeholder input into CER priority-setting, funding, other processes?**
- **Use of cost-effectiveness analysis, other economic analyses under CER?**
- **Timely flow of relevant evidence to decision-makers?**
- **Use of CER findings for coverage and payment decisions by Medicare and other payers?**
- **Establishment of a separate (e.g., private, non-profit) CER institute?**
- **Role of CER in broader US health reform?**
- **Impacts on innovation, value?**

Implications for Life Sciences Industry (1)

- 1. Monitor and participate in developments pertaining to national CER/HTA capacity**
- 2. Evidence standards are not getting any lower; it is particularly difficult to demonstrate, e.g.:**
 - superiority vs. an effective standard of care**
 - causal connection between screening or diagnostic tests and health outcomes**
- 3. Regulatory, payment, other HTA requirements are being joined by further CER evidence requirements**
- 4. Weigh/integrate need to satisfy demand for CER as well as personalized medicine**

Implications for Life Sciences Industry (2)

- 5. Anticipate evidence req'ts throughout technology lifecycle: Who will want what evidence when?**
- 6. How does CER redefine value, steer innovation?
There will be opportunities and shakeouts**
- 7. Consider risk: Do CER? Wait for CER to happen?**
- 8. Keep sight of big picture: CER is just one element of proposed national health reform**