Comparative Effectiveness Research: The Impact of Innovation on U.S. Health Care

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New England Healthcare Institute

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Introduction

Comparative effectiveness research (CER) has emerged as a central issue in the debate over health policy reform in the U.S, as legislation has been introduced to create a major new federally supported program for comparative effectiveness research. It is an issue that holds significant implications for health care innovation, quality and cost.

The New England Healthcare Institute (NEHI) has launched an initiative to identify the implications of CER on innovation and innovation processes across the U.S. health care system. The initiative examines the interplay of CER and innovation from the perspective of multiple stakeholders, including patient groups, physicians, payers, manufacturers and academic researchers. NEHI has developed a broad overview of the issues relating to CER and health care innovation. This issue brief is designed to identify and examine those issues.

Study Approach

This NEHI Issue Brief is based on an extensive literature review, interviews with national experts and thought leaders, and three focus group discussions with participants from across the health care sector.

What is comparative effectiveness research?

Learning what works best

CER in health care entails the comparison of two or more health care interventions. The interventions compared can be discrete (a single drug, a single device), or encompass combinations of products and care practices, or include a review of health care organization, management and delivery. Ideally, the goal of CER is to generate findings on the impact of various interventions in real-world use.

Comparative clinical effectiveness vs. cost effectiveness

Comparative effectiveness is often defined as a comparison of clinical outcomes. However, others use the term more broadly to include cost effectiveness as well. Pending legislation in the Senate would create a new, federally-supported entity to sponsor comparative clinical effectiveness research. Other proposals and programs include *cost* effectiveness or *cost-utility* research that evaluates the economic cost of different interventions in relation to their health benefits.

Historical and current investment in CER

The concept of Federal support for research to “learn what works in health care” is not a new one. Comparative studies are sometimes sponsored by clinical research programs of the National Institutes of Health. The Agency for Healthcare Research and Quality (AHRQ) conducts comparative effectiveness reviews under authority of the 2003 Medicare Modernization Act. The private sector conducts CER through organizations such as Blue Cross Blue Shield’s Technology Evaluation Center (TEC). Previously, such analysis has been pursued at the federal level through entities such as the National Center for Health Care Technology and the Office of Technology Assessment. ‘Lessons learned’ from current and past efforts will be an important element in the ongoing debate on the impact of CER on innovation.

Why is comparative effectiveness research an issue now?

Drive for health care reform and evidence-based medicine

Interest in CER has surged as health care reform and concern about health care costs have once again become a major national issue. Interest in CER is also inspired by the growing movement for health care quality and patient safety, and by evidence (pioneered by Dartmouth's Dr. Jack Wennberg and others) that demonstrates widespread variation in medical practices across the U.S.

As of September 2008, major CER proposals include S.3408, filed by Senators Max Baucus and Kent Conrad. The House passed similar legislation in 2007 as part of the CHAMP bill (Section 904 of HR. 3162), and a comparative effectiveness provision is also included in the Wyden-Bennett health reform proposal (S.334). See Appendix I for details regarding current legislative proposals.

Innovation in U.S. health care

Advances in health outcomes and unmet medical needs

Continued advances in medical technology are credited with significant improvement in health outcomes over the last 50 years: the radical improvement in heart disease treatment and significant gains in cancer mortality are just two well-documented examples. In addition, the U.S has been and continues to be the leading global source of new research, products and technologies to address unmet medical needs.

Cost containment and affordability

Americans broadly support medical innovation. At the same time, policy-makers confront rising health care costs and some view comparative effectiveness research as a possible cost-containment tool. Therefore, it is important to understand the potential effects of comparative effectiveness research (both positive and negative) on medical innovation.

Innovation is a key factor in health care system change

Health care innovation is often equated with advances in new medical technology. But innovation occurs across the health care system in the design, management, financing, and delivery of health care, as well. Even simple improvements in care management processes and even benefit design may yield major advances. Recent examples of significant innovations in health care delivery include the '100,000 Lives' campaign for patient safety executed by U.S. hospitals; the 'Asheville Project' that created significant improvements in diabetes management through partnerships of patients, employers and pharmacists; and the success of major U.S. employers in reducing employee health risks through 'value based' health care benefit design.

How innovation happens: the dynamics of health care innovation

To understand the potential impact of CER on innovation in U.S. health care it is essential to understand how innovation happens. The dynamics of innovation in health care are unique, and perhaps best seen in two categories: innovation in medical technologies, and innovation in health care delivery.

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Dynamics of medical technology innovation

Innovation in medical technology is based largely on scientific advances, and many technology innovations are regulated. Medicines and some medical devices (like higher-risk implants) are highly regulated by FDA, developed over long lead times (12-15 years for new drugs), and subject to prospective clinical research prior to FDA approval for use. Other technologies (like many diagnostic tests, imaging systems, and some surgical equipment) are less heavily regulated but still require FDA review and approval. Surgical and medical procedures are generally not subject to premarket review and prospective clinical research.

Several elements of medical technology development are worth noting from the standpoint of potential comparative effectiveness review:

- Innovations evolve through real-world use
  Typically, the role of medical technology in the care of patients changes over time, with new products and procedures often finding their best, highest-value uses in the months and years after initial introduction. For example, new anti-cancer medicines often are initially approved for late-stage disease, but eventually evolve to be used as first- or second-line treatments. Development of medical devices is frequently iterative, based on a process of clinical adoption, feedback, redesign, use and more feedback (advances in artificial joints and pacemakers are examples). Similarly, medical lasers initially used in ophthalmology and dermatology ultimately were applied in other fields such as gastroenterology, oncology, and thoracic surgery.

- Technologies create value in combination with other technologies
  Frequently, new medical technologies find their best, highest-value use in combination with other products or procedures, and as a result of clinical experimentation with varying combinations over time. Experimentation frequently results in incremental progress in medical treatment that may be difficult to discern in the short term but accumulates over time (as seen in drug and behavior-based hypertension treatment, for example).

- Successful innovations address variation in patient physiology and preference
  Incremental progress in medical treatment is frequently a result of new technologies finding their best applications among patient subpopulations. The clinical and economic value of medical technologies can vary widely among different individual patients and patient subgroups. Advances in genetics are revealing the nature of patient sub-groups at an increasing rate, and thus the extent to which genetic variation plays a role in varying patient responses to treatments. As NEHI focus group participants noted, the emerging field of 'personalized medicine' is a potentially disruptive innovation that holds significant implications for the conduct and application of comparative effectiveness research. See Appendix II for additional discussion of this topic.

  In addition, differences in patient needs and preferences – frequently influenced by socio-economic factors such as educational attainment – often exert a decisive influence on patient access to and acceptance of medical treatments, (for example, in choosing bypass surgery vs. stenting for heart disease, or in maintaining adherence to prescribed therapies). These variations are often critical to identifying the appropriate and most effective treatment for an individual patient.

- Even successful or proven technologies vary in rates of diffusion and adoption
  Rates of diffusion and adoption of innovative medical technologies vary greatly from one class of technology to another. The Institute of Medicine's landmark report on patient safety (*Crossing the Quality Chasm)* estimated that new knowledge gained from randomized clinical trials requires 17 years, on average, to be widely adopted into practice. Meanwhile, new surgical procedures are frequently adopted with little or no clinical evaluation, despite the fact that procedures account for a much greater share of health care spending than regulated products (drugs and devices) subject to randomized clinical trials.

Dynamics of innovation in health care delivery

Innovation at the health system level, including health care design, management, finance and delivery, is driven by a very different set of factors. Technological change is one factor (as witness the development of healthcare IT), but other frequently-cited drivers include reimbursement policy and payment systems, market competition, systems engineering, leadership, and vehicles (such as medical education, guidelines and patient education) that diffuse best standards of practice. High and well-documented rates of practice variation throughout the U.S. are frequently attributed to poorly-diffused standards of practice, payment policies that are not supportive of innovation in health care delivery, and fragmentation among health care providers and health care delivery systems.

Goals of CER

Consensus on goals

There is general consensus that the overarching goal of government-supported CER should be to improve health outcomes through *clinical* effectiveness research.

> "We want to know what works best – when and where and how and for whom."
>
> *- Industry Representative, NEHI Focus Group*

Role of health care costs

Stakeholders from across the health care system, including patients, payers, providers and manufacturers, agree that cost containment should not be a primary goal of CER. First, there is concern by some stakeholders that an overemphasis on achieving cost savings from CER could lead to a skewed research agenda and the potential for sub-optimal application of findings. In addition, for the near-term, introducing economic analysis (e.g., cost effectiveness) as a research goal risks increased politicization and controversy within the effort, undermining the independence and cooperation required to implement a successful comparative effectiveness research process. Stakeholders recognize that CER may impact costs indirectly through the application of clinical effectiveness studies by payers and policy makers and defining care management and organization programs and setting coverage and payment policies. Moreover, a CER program structured around *clinical* effectiveness could still prioritize issues of cost by focusing on study targets that pertain to high-cost disease states or other major drivers of spending.

Implications for innovation

- Clinical effectiveness standard and medical technology
  The consensus around *clinical* effectiveness as the primary goal for CER is broadly viewed as more supportive of medical technology innovation than a cost effectiveness goal would be. Clinical effectiveness studies are seen as more likely to utilize clear, objective methodologies and, when applied, less likely to impede clinical experimentation over the course of a new technology's 'life cycle.'

Scope and priorities of CER

Importance of broadly-scoped studies

CER can be applied to many facets of health care. Stakeholders from across the health care system agree that broadly-scoped CER studies that evaluate a wide range of interventions, including medical technology, care delivery models, clinician practices, protocols and benefit design, will have the biggest impact on the goal of improving health outcomes.

Narrowly-scoped studies: the path of least resistance?

Despite a common vision of broadly-scoped CER studies, some stakeholders point out that current CER activities tend to focus on areas where the evidence base already is the greatest (i.e. medical products that are heavily regulated by the FDA), even in cases where the CER mandate is broad, (such as the mandate given AHRQ through the 2003 Medicare Modernization Act). Conversely, others believe that, because proposals for CER are premised on the need to close evidence gaps, interventions related to organization, management and delivery of care likely will be prioritized for research because of the significant evidence gaps identified in these areas.

Implications for innovation

- Broadly-scoped CER studies are more likely to support innovation throughout the health care system
  Broadly-scoped CER studies are more likely than narrow studies to account for the dynamics of innovation that create value for patients, such as the value created by clinical experimentation with combinations of technologies and medical services. The risk from more narrow, true 'head-to-head' studies is that experimentation with, and adoption of innovations may be constrained because narrow studies may miss the benefits created as a discrete technology evolves through varying applications. Conversely, comparative effectiveness studies may well reward the adoption of innovations that can demonstrate improvements in health outcomes at an early stage in their post-market life cycle.

> "It's just not as simple as looking at discrete technologies."
> *- Payer, Interview*

- CER program priorities that address 'evidence gaps' across the health system are more likely to support innovation throughout the health care system
  NEHI finds a consensus among stakeholders that suggests CER priorities should be based on addressing evidence gaps in health care, and not based on the relative availability of data. Some analysts fear that the availability of data on medical technologies (due in large part to randomized clinical trials) will skew priorities towards research on medical technologies and discrete medical products, while great opportunities for improved health outcomes lie in analysis of health care delivery and systems-level issues.

Methodologies and Process

Methodological Choices

Appropriate methodologies are needed to support CER programs that focus on a broad range of interventions, not just medical technologies, but development of appropriate methodologies is a work in progress (a fact noted in the Baucus/Conrad legislation). Methods for conducting randomized controlled trials are well-established, but such trials are time-consuming and expensive to conduct and are not pertinent to some types of intervention. Other research methods are also available, including registries, claims or medical record analysis, and inferential modeling, but each presents challenges in ensuring validity of results.

Transparency

Since development of appropriate CER methodologies is a major challenge, transparency will be a challenge as well. The validity of CER findings will depend in large part on whether major stakeholders reach a consensus view on CER methods.

Timing

As noted earlier, innovations across the health care system frequently find their best and most valuable uses over a 'life cycle' that includes a period of clinical experimentation and use. Health care system experts, physicians, payers and innovators alike express concern that CER reviews, in their current form, typically examine an innovation at a single point in time, which cannot fully capture the future value of that innovation. An important issue for CER policy will be finding the right time(s) in an innovation's 'life cycle' to evaluate it and/or finding a flexible system that will enable reviews to be ongoing or evolutionary in their findings.

Implications for innovation

- Selection of Methodology
  Methodological issues in comparative effectiveness research could hold significant implications for medical innovations and how those innovations are made available to patients. For example, if strong, well-established research methods are not available, this could lead to a "moving target" for research and increase unpredictability for medical researchers and innovators alike.

- Investment in appropriate methodologies
  A lack of dedication to addressing methodological issues might cause CER programs to default to subsets of medical interventions for which methods are strongest. Stakeholders agree that inadequate investment in methodological development would diminish the overall impact of CER on improving health outcomes. Conversely, strong and successful investment in new methodologies presents an opportunity to close what many observers believe is a growing 'translation gap' in U.S. medicine, or a gap between a growing volume of new medical knowledge sparked by scientific advances, and its transfer into useful interventions and ultimate adoption by clinicians and patients.

> "The politics are way ahead of the methodologies."
> *- Academic Researcher, Interview*

- Transparency
  Transparency will enhance predictability of CER programs and foster "buy-in" and credibility to CER findings, minimize conflict among stakeholders, and maximize the likelihood that findings will be disseminated and utilized appropriately. Transparency is particularly crucial to 'upstream' innovators of new medical technologies who face long and costly lead-times for the development of new products and need to make early and sound go/no-go decisions.

- Synchronization of CER and the innovation 'life cycle'
  Determining the appropriate time in an intervention life cycle to conduct CER studies will be important. Studies should focus on innovations that have had time to 'prove themselves' through clinical experimentation and use; studies conducted too early may inadvertently cut off innovation. If studies are flexible and life cycle is taken into consideration, CER will continue to permit important innovation in the laboratory and in patient care.

Potential Applications

Dissemination of findings

Whatever policy decisions are made on CER goals, scope and methodologies, CER will have little impact on medical decision-making or health outcomes, unless the findings are disseminated and used appropriately within the health care system. How CER findings will be communicated and applied will be a critical factor in CER's impact on innovation throughout the health care system.

Form of findings

Current comparative effectiveness legislation calls for CER studies conducted by government supported programs to be advisory, providing information to support decision-making by physicians, patients, payers and others. Current proposals do not envision converting government-supported CER studies into blanket or nationwide coverage decisions on new technologies or medical practices.

Communication to consumers, patients and providers

Effective adoption of findings by providers, patients and consumers requires CER findings – which often are subtle and complex – be communicated in ways that are timely, accurate and simple. The U.S. track record for adoption of existing forms of evidence-based medical advice (such as clinical practice guidelines) is mixed – as demonstrated by the Institute of Medicine's finding that fundamental evidence-based findings still require 17 years, on average, to achieve widespread adoption.

Implications for coverage and reimbursement

NEHI finds that stakeholders believe that payers will incorporate CER findings into the larger body of information they routinely use to make coverage and reimbursement decisions. However, payers may well decide to reward utilization of interventions that demonstrate not only superior effectiveness, but lower costs. Utilization incentives might include use of tiered deductibles and lower co-pays for patients, and performance incentives for providers (pay for performance).

Implications for Innovation

- Flexibility in patient and clinical decision-making
  To sustain innovation across the health care system, most stakeholders believe that CER findings should be informative, but not prescriptive; that is, they should inform patient and physician decision-making, but allow for treatment decisions that are most appropriate to the individual patient and situation.

- Flexibility in payer decision-making
  One of the greatest risks to innovation is that CER, even in an advisory-only form, becomes a singular tool to make coverage decisions. The concern is that such a standard could become a rigid barrier to market entry and may negatively impact medical innovation and the resulting benefits to patients. Stakeholders generally agreed that to support continued innovation, payers should not apply CER findings in ways that use findings as the basis for "on/off" coverage decisions, which could cut off access and clinical experimentation to promising new technologies or care management processes that may evolve over time and find new applications in different populations and diseases.

> "Simple on/off decisions may disrupt innovation and best practices at the point of care."
> *- Provider, NEHI Focus Group*

Conclusion

Comparative effectiveness research will likely have significant implications for both the rate of innovation and the type of innovations within U.S. health care. As policy-makers consider expansion of CER, it will be important to do so in ways that achieve the dual goals of supporting continued medical progress and realizing the benefits of additional comparative effectiveness research.

Among the critical factors relevant to a balanced approach to CER and innovation:

- Goals
  Critical issues identified by NEHI is this area include whether the CER program's goals are centered on quality improvement or cost containment, and whether the program encompasses clinical outcomes or also includes economic outcomes. Stakeholders interviewed by NEHI generally support *clinical* effectiveness as the best goal for CER, in part because CER studies focused on clinical effectiveness are more likely to support innovation than CER conducted for goals such as cost-effectiveness.

- Scope and Priorities
  A second key issue is whether the scope of the CER program includes medical technologies and procedures, or also includes interventions related to organization, management and delivery of care. In NEHI's research, CER studies with broad scopes of study (not a focus on discrete products and services) were viewed as more likely to support innovation, particularly innovation in care delivery and health care system improvement. Innovation will also be sustained if CER priority-setting encompasses 'downstream' issues in health care delivery.

- Methodologies and Process
  The most robust research methodologies and data available today pertain mostly to medical technologies. New CER programs will need to make a strong commitment to the development of new methodologies and data sources in order to support CER goals and priorities.

- Potential Applications
  Stakeholders agreed that approaches to applying CER findings will have a critical impact on innovation. CER findings that inform the decisions of patients, providers and payers are more likely to sustain (while nonetheless influencing) innovation, while findings used to make 'on/off' decisions hold greater risk for discouraging innovation. CER findings will need to find an audience among patients, providers and payers if they are to drive needed innovation in the health care system – so innovation in the dissemination and adoption of findings is a key priority itself.

APPENDIX I
Selected Comparative Effectiveness Legislation in the 110th Congress

S. 3408 Comparative Effectiveness Research Act of 2008 (Baucus/Conrad)
Establishes the Health Care Comparative Effectiveness Research Institute as a private, non-profit corporation. The Institute will identify research priorities, support data collection, new studies, and methodology development. The Institute is funded from the Medicare Hospital Insurance Trust Fund and fees on fully-insured and self-insured health plans.

H.R. 3162 Children's Health and Medicare Protection Act of 2007 (Dingell)
Establishes a Center for Comparative Effectiveness Research within AHRQ, responsible for conducting and supporting CER research. An independent commission is created to oversee the program. The Center is funded through Medicare Trust Funds and fees on fully-insured and self-insured health plans.

S. 334: Healthy Americans Act (Wyden)
Establishes a Comparative Effectiveness Advisory Board charged with making recommendations on research priorities, the conduct and dissemination of CER findings, and the creation of comparative effectiveness research centers. The Board is funded through Medicare Trust Funds and through fees on health insurance policies.

H.R. 2184: Enhanced Health Care Value for All Act of 2007 (Wasserman-Schulz)
Substantially similar to S. 334 (above)

S. 3 Medicare Prescription Drug Price Negotiation Act (Reid)
Creates no new entity, but proposes creation of a prioritized list of clinical effectiveness studies critical to building evidence that support value-based purchasing of Medicare Part D drugs. Funding is unspecified.

S. 2988: Accelerating Cures Act (Lieberman)
Creates a Federally-funded Research & Development Center (FFRDC) on comparative effectiveness. The center reviews and disseminates studies, sets priorities for research, funds clinical trials, and develops methodological standards. Funding is unspecified.

H.R. 6331 Medicare Improvements for Patient and Providers Act (Rangel)
No new entity is established. The legislation requires HHS to contract with IOM to report on best practices for the conduct of systematic review and the development of clinical guidelines. Funding is from monies 'not otherwise appropriated.'

APPENDIX II
Can CER support innovation in the field of personalized medicine?

A new paradigm of innovation termed "personalized medicine" is emerging in health care in which advances in genomics and other biological sciences are driving the creation of highly targeted tests and therapies tailored to the genetic characteristics of individual patients and subpopulations. Personalized medicine draws on information from a range of sources (including individual genetic variation, differences in molecular-level and cellular-level disease processes, health states, behavioral and environmental determinants and response to interventions) to tailor care strategies and treatments to the needs of individuals, and also to facilitate the discovery and validation of health care products and other interventions. The goal is delivery of "the right treatment to the right patient at the right time."

Efforts to "learn what works best" in health care through comparative effectiveness research could support personalized medicine, which is also evidence-driven. For example, CER could provide new avenues for strengthening the evidence base for gene-based diagnostic tests, which sometimes lack evidence of clinical validity. Better evidence about care management and coordination also could foster health care delivery pathways that support adoption of personalized medicine tests and treatments.

Other the other hand, CER is oriented towards population-based evaluations and applications of evidence, whereas personalized medicine occurs at the level of sub-populations and individual patients. Thus, depending on how CER studies are conducted and applied, they also could pose a barrier to the emergence of personalized medicine.