

## Incentivizing Comparative Effectiveness Research

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### Abstract

Comparative effective research (CER) compares alternative methods of preventing, diagnosing, treating, and otherwise managing medical conditions. The Patient Protection and Affordable Care Act authorized creation and funding of an independent agency, the Patient-Centered Outcomes Research Institute, to expand CER in the U.S. A key issue in the years ahead is the extent to which public investment in CER and related initiatives should be further expanded in an attempt to improve the efficiency of healthcare spending, limit cost growth, and reduce projected deficits for Medicare and Medicaid. This study provides an overview and analysis of public funding of CER and the desirability and feasibility of incentivizing additional CER in the private sector. It explores key impediments to higher private spending on CER, the rationales for increased public investment, the potential benefits and inherent limitations of publicly-funded CER, and the advantages of pursuing a multifaceted approach to increase private sector, entrepreneurial investment in CER.

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## **I. Introduction and Summary**

Comparative effective research (CER) compares alternative methods of preventing, diagnosing, treating, and otherwise managing medical conditions. The basic goal is to provide rigorous evidence of the relative effectiveness of different methods. Although precise estimates are not available, current spending on CER represents a very small fraction of U.S. healthcare spending. For example, total CER spending was estimated at less than \$1.5 billion in 2005, compared with total healthcare spending in 2009 of roughly \$2.4 trillion, representing 17 percent of GDP and about \$8,000 per person.<sup>1</sup> Many policymakers and experts argue that substantial expansions in CER would have the potential to reduce significantly the growth rate in U.S. healthcare spending – while improving the overall quality of care.

The American Recovery and Reinvestment Act (ARRA) of 2009 authorized federal expenditures of \$1.1 billion to fund CER. The Patient Protection and Affordable Care Act of 2010 subsequently authorized creation and funding of an independent agency, the Patient-Centered Outcomes Research Institute, to fund and otherwise support CER. The prevalent theoretical justification for public funding is that CER findings constitute a public good for which private incentives for production are less than socially optimal. The ensuing lack of evidence concerning the merits of alternative medical treatments in turn results in suboptimal medical care and excessive spending on treatments that are not based on scientific evidence.

Substantial interest in increased public investment in CER reflects general concern with developing appropriate policies to address high and rapidly growing U.S. healthcare spending and the enormous long-term fiscal burdens projected for Medicare and Medicaid.<sup>2</sup> According to the Institute of Medicine (IOM), less than half of medical care provided in the U.S. is based on evidence of what works.<sup>3</sup> A lack of evidence on effective care and research on regional variation in Medicare spending have provided significant impetus to proposals for increased government spending on CER in general and for the CER provisions in the ARRA and PPACA in particular. Research on regional variation documents substantial variation in Medicare spending across regions, due primarily to differences in the amounts of medical care provided for similar conditions. While not unequivocal, other research suggests that much higher spending in some regions is not associated with higher quality medical outcomes and that higher spending in some cases might be associated with worse health outcomes.<sup>4</sup> These findings have led some researchers, observers, and policymakers, including President Obama and former Director of the Office of Management and Budget, Peter Orzag, to posit that higher Medicare spending could be reduced by up to 30 percent annually without reducing quality of care and to propose increased spending on CER as a means to achieve those savings. More generally, by providing more and better evidence of what works

best, it is hoped that CER will encourage patients and providers to curtail costly yet ineffective treatments while improving health outcomes.

As is true for all proposals that affect U.S. healthcare spending, increased public spending on CER has generated controversy and resistance. Concern has been expressed about the “public good” rationale for increased government spending; the likely timeliness and impact of CER; the possibility of unintended, adverse health effects; the potential effects of rent seeking and political pressure on the types of CER that are publicly funded; possible crowding out of private CER; and the potential evolution of public spending on CER toward regimes where government-sponsored CER is used to make coverage decisions under Medicare and/or private insurance.<sup>5</sup> There is also concern that government funded CER will gravitate toward “cost effectiveness” analysis, which considers the relative effectiveness of different forms of medical care in relation to the costs of providing care, and again be used to decide what forms of care are reimbursed by government and private insurance.

Given this context, a key issue confronting citizens and policymakers in the U.S. in the years ahead is the extent to which public investment in CER and related initiatives should be expanded in an attempt to improve efficiency of healthcare spending, limit cost growth, reduce projected spending on Medicare and Medicaid. This study addresses this issue by providing an overview and critical analysis of public funding of CER and alternative methods of promoting CER. The study emphasizes the desirability and feasibility of incentivizing increased private investment in CER, as either an alternative or complement to public spending. It explores key impediments to higher private investment in CER, the rationales for increased public investment, the potential benefits and inherent limitations of publicly-funded CER, and the advantages of a multifaceted approach to incentivizing increased private investment.

The study makes three principal arguments. First, given the complexity and dynamism of modern healthcare and the inherent limitations of public investment in CER, it is desirable to encourage substantial and diverse private sector investment in CER. Second, although the public good characteristics of investment in information reduce private incentives for investment in CER, a more important impediment is the reduction in demand for CER attributable to the design of government and private health insurance and associated provider reimbursement. Third, even apart from the disincentives for CER from the insurance system, careful attention should be paid to possible policies for subsidizing CER without direct government funding and allocation of CER funds. In particular, consideration should be given to promoting the open availability of research data on medical treatments and health outcomes and to expanding tax incentives to promote decentralized, non-governmental investment in CER. The overall conclusion is that well designed policies to increase incentives for private sector CER have the

potential to increase substantially the evidentiary basis of medical decisions, including the stimulation of entrepreneurial investment in innovation to guide such decisions.

The analysis begins with detailed background on the objectives, nature, and methods of CER, how CER differs from cost effectiveness analysis, and factors influence whether increased spending on CER will reduce healthcare spending. The next section examines public and private CER in the U.S., including provisions in the PPACA, followed by discussion of public systems of promoting CER and related analyses in selected countries. Given this background, the study then examines in greater detail the rationales for and limitations of increased public spending on CER. The final section considers broad strategies for incentivizing private investment in CER as an alternative or complement to public investment.

## **II. Background**

### *Defining CER*

A variety of definitions of CER have been offered, including in a 2007 report by the Congressional Budget Office (CBO) and a 2009 report by the Institute of Medicine (IOM).<sup>6</sup> The definitions vary in the types of analysis included, whether CER encompasses consideration of costs, and specific aspects of health care delivery that will be subject to CER. The IOM report defines CER as follows:

Comparative effectiveness research (CER) is 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.

This definition encompasses a broad range of activities and indicates that CER should consider patient-focused, individualized care in addition to care at the population level. The IOM definition and the provisions regarding CER in the ARRA and PPACA (see below) exclude formal cost-effectiveness analysis (the extent to which benefits exceed costs) under the CER rubric.

The concept of “effectiveness” in CER is distinct from the concept of “efficacy.” Clinical research in the development of pharmaceuticals, biologics, and often medical devices is generally designed to demonstrate efficacy – whether the product has a therapeutic benefit relative to a placebo – under highly controlled conditions. The Food and Drug Administration (FDA) requires studies of efficacy (usually based on randomized controlled trials, or RCTs) in order to determine whether or not to approve a product for use in the U.S. market. Studies of efficacy usually examine whether or not the product works in patients who are selected under strict study protocols; for example, participants generally are not allowed

to have comorbid conditions to facilitate conclusions regarding causality (whether the intervention causes improvement).

Assessments of efficacy do not consider how well the product or intervention performs relative to comparators, or what is denoted “effectiveness” in CER. The fundamental distinction is that CER compares a particular intervention with alternative interventions to assess which has the greatest therapeutic effect. While CER may involve RCTs, it often will rely on real-world settings to see how the treatment or product works for patients under more realistic conditions, including the presence of comorbidities. CER involves the comparison of two or more treatments or interventions and generally requires selection of a baseline comparator (or comparators). When specific therapeutic alternatives exist, selecting one (or several) as the benchmark may affect the findings and statistical inference. In some cases, an appropriate comparator may be no treatment or watchful waiting, in which the patient’s condition is simply monitored for a period of time. The IOM report suggests that the best approach may be for the baseline comparator to reflect current best (“optimal”) practice.

#### *Methods for Evaluating Comparative Effectiveness*

Numerous methods are available for evaluating the comparative effectiveness of treatments and interventions.<sup>7</sup> Each may be appropriate under certain circumstances, which vary based on the product or intervention of interest, the relevant comparators, the targeted patient population, and other factors. Some observers stress the desirability of basing CER on specific infrastructure and guidelines for when each method should be used and for conducting trials effectively and efficiently, recommending that initial public funding include a significant component to that end.<sup>8</sup> They argue that establishing and fostering agreement among researchers over appropriate methods and how and when each should be employed will help inspire confidence in the CER process and findings among major stakeholders, which in turn will enhance dissemination and take up of CER findings.

**Randomized Controlled Trials.** The most rigorous methods for conducting CER are experimental and ideally control all aspects of the experiment. The randomized controlled trial (RCT) is considered the “gold standard” for experimental design. Patients are randomly assigned to either the treatment group or alternative (control) group in a highly controlled setting. The alternative of interest can range from a specific “active comparator,” to a “placebo, no intervention, or the standard of care.”<sup>9</sup> The RCT can provide the “most-definitive results” of any design because all aspects of the trial are closely controlled to yield convincing evidence of causal results for the group studied (known as internal validity).

RCTs, however, have a number of drawbacks for use in CER. They do not address whether a particular treatment is better than another treatment in less than “near-ideal circumstances.”<sup>10</sup> As a result, RCTs may have limited external validity: the results of may be inapplicable to populations beyond those considered in the trials. External validity is central to CER, where the overarching goal is to provide comparative evidence of how interventions work in non-experimental settings. RCTs also involve large costs and may take several years to complete. The time required to conduct trials increases the risk that the results will be obsolete by completion given the possibility of treatment innovations that are not compared in the trials.

**Practical Clinical Trials.** “Practical” clinical trials are an alternative to RCTs designed to provide evidence of an intervention’s risks, benefits, and/or costs in routine clinical practice.<sup>11</sup> They generally are conducted with patients with comorbid conditions and diverse demographic backgrounds in a community setting without strict adherence to an RCT protocol. Practical clinical trials can thus provide evidence of the relative effectiveness of treatments for patients not specifically pre-selected for participation in the trial. They have the potential to be more informative than RCTs in some situations, such as identifying the effects of drug interactions and inappropriate use or administration.<sup>12</sup> However, because practical clinical trials trade off the strictly controlled setting of a RCT in favor of findings that may apply in more realistic settings, it can be difficult to attribute causality to the treatment.

**Systematic Reviews.** Systematic reviews collect, summarize, and synthesize the results of various studies (usually RCTs, but also observational studies), to compare one treatment, device, or procedure against another. The reviews employ explicit methodologies and are a transparent means of providing clinicians and patients with information on comparative effectiveness. Because systematic reviews do not involve the generation and analysis of new data, they are relatively inexpensive to conduct and less time consuming than experimental trials. Systematic reviews can also highlight where evidence is lacking. They are, however, limited to existing research.

**Observational Studies.** Retrospective empirical analyses of data on medical treatments and outcomes, known as observational studies, represent a growing and potentially informative source of CER.<sup>13</sup> Analyses can be conducted using extensive databases containing hundreds of thousands or even millions of medical claims. Analysis of claims data enables researchers to obtain results based on significant amounts of data and outcomes at relatively low cost, which may allow addressing issues not amenable to RCTs and/or decisions that do not require the threshold of evidence provided by RCTs.<sup>14</sup>

Medical claims data pose challenges for their use in CER. The lack of randomization of the study population makes it difficult to draw causal inferences regarding the effects of interventions. In addition, patients’ pre-treatment health status often is not captured in claims data, making it difficult to control for

health status as a confounding factor in assessing the effects of a given treatment. Medical registries, in which governments and other entities track the health care utilization of patients with a specific disease, represent another source of data for CER. Unlike claims data, medical registries can capture information on illness severity, allowing researchers to control for variations in severity when analyzing the effects of interventions. Medical registries also allow better measurement of outcomes compared with claims data. If medical registries reflect voluntary participation by patients, however, bias can be introduced from the selection of particular types of patients into the registry. In addition, the length of time required to obtain the appropriate number of participants needed to for analysis can be extensive.

**Model Simulations.** CER can employ decision models to simulate the effects of treatments on different patient populations.<sup>15</sup> Decision modeling combines evidence from a variety of sources with assumptions about how the treatment might work in practice to project its effects. The use of models generally has relatively low cost, but the results depend on numerous assumptions. The models also can be complex and difficult to understand, reducing confidence in the results and the ability to inform clinicians and patients as to the comparative effects of varying treatments.

**Populations and Subgroups.** Regardless of the specific methodology chosen, CER findings typically are representative of the “average” patient. If the research is not focused sufficiently on specific patient characteristics, the findings will not provide enough information to guide clinicians to the “best” treatments. In order to be more helpful, most observers argue that CER should seek to assess effectiveness for sub-groups of patients based, for example, on clinical and socio-demographic factors.

#### *Extending CER to Consider Cost-Effectiveness*

A key issue in the debate surrounding CER, and how to best incorporate it into the U.S. health care system, has been whether costs should also be taken into account when comparing treatments.<sup>16</sup> Cost-effectiveness analyses consider comparative effectiveness and costs of different treatments. The goal is to provide evidence of which interventions provide the most health benefit per dollar of expenditure. Some observers argue that the expanded use of cost-effectiveness analysis is desirable and/or inevitable to limit growth in U.S. medical costs.<sup>17</sup>

The key additional step involved in cost-effectiveness analysis is to measure cost compared with a measure of health benefits provided by a given treatment. Cost-effectiveness analysis usually measures benefits in specific units, such as quality-adjusted life years (QALYs, the estimated additional life expectancy from the intervention adjusted for the estimated adverse effects of medical conditions on the quality of life).<sup>18</sup> Such measurement requires numerous and controversial assumptions and evidence on the average value of a year of additional year of life with and without various medical conditions. Costs

also can be difficult to measure, and the specific costs incorporated in the analysis can vary widely depending on the perspective chosen (e.g., societal costs or health plan costs).<sup>19</sup>

In principle, incorporating costs into the analysis of comparative effectiveness could help focus resources on treatments and interventions that provide greater value for the money. But conducting and using formal cost-effectiveness analysis in treatment and insurance coverage decisions is highly controversial.<sup>20</sup> Cost-effectiveness analysis raises the prospect of formal rationing of medical care because it costs too much. Similarly, because the results of cost-effectiveness analyses may not adequately capture the value of interventions for certain population subgroups, there is concern that it could result in denial of valuable treatment to those groups. The methods used in cost-effectiveness analyses also are generally more controversial than those used for CER. Broad variations in study design and measurement can result in large variations in estimated cost effectiveness, reducing confidence in the results.

The concept of cost-effectiveness is central in the economics of health care. Some observers argue that a centralized government system for comparing cost-effectiveness is desirable in addition to or as part of CER. A more common view is that cost assessments and judgments of benefits in relation to costs should be left to patients, physicians, and, more controversially, private insurers, and there presently is little public and political appetite in the U.S. for government sponsored cost-effectiveness analyses.<sup>21</sup>

#### *Will CER Reduce Healthcare Expenditures?*

The hope that more CER will reduce healthcare expenditures has provided significant impetus for increased government funding of CER. Considerable uncertainty exists about the extent to which this hope will be realized, and it generally is recognized that any savings achieved will require a number of years following expanded public funding. The CBO projects the CER funding in the PPACA will have relatively little effect on federal healthcare spending during its 10-year budget horizon, and the CMS Office of the Actuary projects that these provisions will have little effect on total healthcare spending.<sup>22</sup>

Substantially larger CER investments would not necessarily produce significant savings in healthcare expenditures. The extent of savings for a given expenditure will depend on how many costly treatments are shown to be less effective than lower cost options and on whether and how rapidly the findings influence medical practice.<sup>23</sup> Although the literature on regional variation in healthcare spending suggests that more intensive and costly treatment might not produce significant improvements in health, it is not clear that publicly funded CER will identify specific sources of significant savings. If, for example, certain types of new and costly treatments are shown to be more effective than older, less expensive treatments, CER findings could increase healthcare spending. The CBO's 2007 report and others have



suggested that if developers of treatment innovations had to demonstrate comparative effectiveness (or knew that innovations would be subject to CER), they would increase emphasis on treatments that would meet comparative effectiveness criteria. Other observers have expressed concern that extensive public investment in CER and the attendant increase in uncertainty for developers could adversely affecting innovation and health.

### **III. CER in the U.S.**

#### *U.S. Government Initiatives*

Medicare notwithstanding, the U.S. government has engaged in a variety of efforts to promote CER.<sup>24</sup> The Veterans Administration and Medicaid programs have made significant strides towards the use of CER in benefit design and funding decisions. The 2009 stimulus package and the 2010 health reform legislation increased funding for CER and established the first steps towards the creation of a centralized research organization with the specific mandate of funding CER.

**NIH and AHRQ.** The National Institutes of Health (NIH) is an agency of the U.S. Department of Health and Human Services (HHS) for conducting and funding biomedical and health-related research, with a 2010 budget of \$31.2 billion.<sup>25</sup> The majority of NIH funding is awarded through a competitive grant system to domestic and international researchers. A smaller percentage of funds is retained to conduct research within NIH institutes. Although NIH spending on CER cannot be readily categorized, it funds numerous studies involving primary CER. The agency funded 463 CER studies in fiscal year 2008.<sup>26</sup>

The Agency for Healthcare Research and Quality (AHRQ) is a complementary agency to the NIH within HHS, with 2010 budget of about \$3.5 billion, which focuses on the quality, safety, and efficiency of health care. AHRQ supports health services research and promotes evidence-based decision-making.<sup>27</sup> The agency's research priorities include patient-centered health, prevention and care management, value, health information technology, and patient safety. AHRQ has a dedicated program for funding and tracking CER. Funding for CER studies for fiscal years 2006-2009 ranged from \$13 million to \$35 million annually, with 12-18 studies funded per year.<sup>28</sup>

**The Veterans Administration.** The Veterans Administration (VA) has been conducting CER and implementing the findings into practice for many years.<sup>29</sup> A centralized staff-model structure at the VA enables researchers to access data from a variety of sources, and researchers (about 70% of practicing clinicians with the VA) have access to a clinical research network. There are mechanisms in place for information dissemination, allowing the results of comparative effectiveness analyses to be broadly

released within the VA system. The centralized structure facilitates monitoring of compliance with any new coverage or payment rules based on CER results.

**Medicaid.** Some state Medicaid programs have used CER or cost-effectiveness analyses to make coverage and payment determinations.<sup>30</sup> The most notable example is the State of Oregon, which in 1989 began establishing coverage rules based on the relative value of a given service. The relative value scale took into account both effectiveness and cost within the limitations of the state health budget. A commission was established to create coverage priorities with public input. Based on those priorities and evidence from scientific studies and expert opinion, the commission established an ordered list of about 700 “condition-treatment pairs.” A cutoff is established in view of the state’s Medicaid budget for a two-year period. Treatments above the cutoff are covered; those below are not. While controversial, the policy persists, with Medicaid coverage in Oregon provided to over a million enrollees.

**Medicare.** Medicare bases its coverage decisions on whether care is “reasonable and necessary.” The main criterion for coverage is general clinical effectiveness, not comparative effectiveness. Coverage of new treatments is determined either locally through regional Medicare contractors (often affiliated with private insurers) or through a national coverage decision by the Center for Medicare and Medicaid Services (CMS). While a number of presidential administrations have sought to interpret the “reasonable and necessary” criterion as requiring evidence of comparative effectiveness, those attempts have met political opposition and been unsuccessful. Since 2003, and pending specific developments under CER provisions in the health reform law discussed below, Medicare has been restricted by law from using CER to make coverage decisions.<sup>31</sup> Medicare recently began to extend coverage to treatments with insufficient evidence to support coverage if the patient enrolls in a clinical trial or registry with the goal of establishing additional evidence that will help in the coverage determination process.

**CER in the Stimulus and Healthcare Reform Bills.** The American Recovery and Reinvestment Act of 2009 (ARRA) provided \$1.1 billion for CER to the HHS (including \$300 million to AHRQ and \$400 million to NIH) to support efforts to:

- . . . (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 . . .

The ARRA established the Federal Coordinating Council for CER to coordinate federal efforts and advise the administration on CER needs and appropriate infrastructure. The 15-member Council submitted a report on existing CER, resources, needs, and priorities in June 2009. The ARRA also

required the IOM to issue a report to Congress and the HHS on priorities for research in comparative effectiveness, which was also submitted in June 2009.

The Patient Protection and Affordable Care Act (PPACA), enacted into law in March 2010, formally terminated the Federal Coordinating Council for CER and created the Patient-Centered Outcomes Research Institute (PCORI). The statutory mission of the PCORI is to advance the “quality and relevance of evidence” available for patients, physicians, and payers. The PCORI is responsible for identifying research priorities, analyzing evidence, identifying the relevance of current evidence and economic effects, and disseminating research findings. The PCORI will pursue “comparative clinical effectiveness research,” described as head-to-head comparisons of “interventions, protocols of treatment, care management, and delivery, procedures, medical devices, diagnostic tools, pharmaceuticals (including drugs and biologicals), integrative health practices, and any other strategies or items being used in the treatment, management, and diagnosis of, or prevention of illness or injury.”<sup>32</sup> The PCORI will submit a draft of research priorities for public comment prior to formal adoption. The assessment will be independent of the previous assessment by the Federal Coordinating Council and IOM.

The PCORI is a non-profit organization, independent of any government agency and directed by a Board of Governors composed of the heads of the NIH and AHRQ and 19 other nominated members selected by the General Comptroller. Initial appointments to the Board of Governors were made in September and October, 2010. By statute, three board members must represent patient and consumer interests. There must be seven physicians and provider representatives including at least one surgeon, nurse, integrative healthcare practitioner, and hospital representative. Three private payer representatives, including at least one to represent health insurers and another to represent self-funded employers who self-insure, are required. Biopharmaceutical and medical device firms have three representatives. One board member is required to be an independent health service researcher; two members must represent state or federal health agencies.

The PCORI’s research methodology and scope will be guided by the NIH and the AHRQ. A Methodology Committee of up to 15 members will be appointed by the General Comptroller to develop a standard of evidence and review for all research funded through the PCORI. The Methodology Committee, to be announced in early 2011, is expected to consist of experts in the fields of “health services research, clinical research, CER, biostatistics, genomics, and research methodology.” Its recommendations will be submitted to the Governors’ Board for adoption.

The PCORI will be funded by direct appropriations of \$10 million, \$50 million, and \$150 million during fiscal years 2010-2012, respectively. Funding for fiscal years 2013 to 2019 will be from a trust that will receive annual direct appropriations of \$150 million and per capita charges (estimated at \$2)

from enrollees in Medicare and privately insured and self-insured health plans. The projected value of these charges is estimated to exceed \$500 million. No funding provisions have been made for years following 2019. The trust will fund research by government, academic, and private agencies, with preference given to AHRQ projects and NIH projects that fall within the PCORI's guidelines.<sup>33</sup>

PCORI-funded researchers will have access to CMS data for beneficiaries of Medicare, Medicaid, and the Children's Health Insurance Program. Researchers will also have access to data collected under the Public Health Act for diagnosed cases of infectious disease and emergency department visits. The PCORI has the right to request data from federal, state, and private entities. Completed research must be submitted to a peer-review process and released within 90 days to the public. The dissemination of research results will be assisted by AHRQ's Office of Communications and Knowledge Transfer. Efforts have begun to develop informational media for patients, providers, and payers. The AHRQ will separately maintain a public-access database of government-funded CER. Researchers who enter into a data-use agreement with PCORI are permitted to publish their findings in peer-reviewed journals. The PCORI is also expected to identify evidentiary gaps that may be addressed with new, related research.

The PPACA places limitations on the use of findings from PCORI-funded CER in Medicare coverage decisions.<sup>34</sup> The findings cannot be construed as mandates, guidelines, or recommendations for payment, coverage, or treatment. Coverage cannot be denied solely on the basis of CER. Evidence from CER can only be used as part of a larger process for making coverage decisions: it cannot be used without "an iterative and transparent process which includes public comment and considers the effect on subpopulations." The PCORI is specifically prohibited from adopting a QALY or similar threshold for establishing what types of care are cost effective, and Medicare coverage decisions cannot be made in a manner that "treats extending the life of an elderly, disabled, or terminally ill individual as of lower value" than an individual "who is younger, non-disabled, or not terminally ill." The law also states that nothing in its CER provisions should be construed as "superceding or modifying the coverage and services" that the HHS Secretary "determines are reasonable and necessary" under existing law.

#### *Private Sector Initiatives*

Numerous private (non-governmental) entities in the U.S. are involved in conducting CER and related research, including coordinated efforts among payers to improve quality through CER. In conjunction with rapid growth in high deductible health plans, in significant part associated with Health Savings Accounts and related plans, there has also been substantial growth in the provision of information to guide consumers' decisions regarding medical care and choice of providers.

The Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) is the most prominent example of disseminating information on evidence-based medical practices in the U.S. Established in 1985, the TEC has developed scientific criteria for assessing medical technologies and maintained a database of its Health Technology Assessments (HTAs).<sup>35</sup> The TEC provides HTAs to Blue Cross and Blue Shield Member Plans and Kaiser Permanente plans. All reports are publicly available online. The scope of analysis is limited to clinical effectiveness; it does not encompass comparative effectiveness. While the assessments are intended to inform coverage decisions, they are not directly connected to coverage decisions. A major function of the assessments is to provide information to private insurers that a technology is no longer experimental or investigational, which significantly increases the likelihood of coverage among private insurers.<sup>36</sup>

Private health plans have also collaborated in the contribution of data to facilitate the consideration of CER in coverage decisions. The HMO Research Network, for example, is a multi-payer effort to identify effective care. Formed in 1993, participating HMOs pool claims data and support independent research concerning comparative effectiveness. The research is peer-reviewed and publicly available. The data base is a major source of information for research networks focusing on effective treatments for cancer, cardiovascular diseases, and therapeutics (HMO Research Network, 2008).

Another private entity that provides information regarding comparative effectiveness is the Institute for Clinical and Economic Review (ICER) at the Institute for Technology Assessment at Massachusetts General Hospital. ICER rates both clinical effectiveness and comparative value of health care treatments. It utilizes a copyrighted rating system, the ICER Integrated Evidence Rating<sup>TM</sup>, which combines ratings of clinical effectiveness and “comparative value” based on systematic reviews and economic modeling. The ICER clinical effectiveness rating is based on the credibility of supporting evidence of therapeutic effects and the net health benefit.<sup>37</sup> The comparative value rating is based on judgment in consideration of multiple metrics of value. The ICER review process involves a scoping committee, followed by a meta-analysis of the current research available, and submission of a report to an independent Evidence Review Group composed of field experts, patient representatives, health economists, and policy advisors. If a rating decision is not unanimous, the final report includes a breakdown of the committee vote. The ICER is funded from a variety of sources, including many health insurance plans. The assessments and ratings are available free of charge online.

A variety of subscription-based services provide access to consultant reports about health interventions. For example, Hayes, Inc., one of the largest medical technology research and consulting firms, provides systematic reviews and evaluations of medical and surgical procedures, drugs, and devices on a fee or subscription basis to private health plans and healthcare systems.<sup>38</sup> Hayes conducts health

technology assessments, technology consulting services, and employee education seminars regarding the practice of evidence-based medicine. As another example, the Emergency Care Research Institute, formed in 1968, initially focused on best practices in an emergent care setting. It expanded in the early 1970s to include technical assessments of a broad array of medical interventions. Clients include hospitals, government agencies, and private health plans.<sup>39</sup> The organization also provides information to the public without charge concerning safety and medical technology, including a Patient Safety website, access to a Medical Device Problem-Reporting database, and access to some of its proposed health technology assessments. In June, 2010, Medicalis Corporation announced the launch of an integrated technology platform to provide clinical decision support and quality tracking to enable comparative effectiveness assessments in medical imaging, including more than 30 quality measures and tracking of adherence to patient safety standards and compliance with clinical guidelines.<sup>40</sup>

A variety of non-profit CER initiatives take the form of data and research registries. One prominent example is the Cochrane Library, which includes several databases devoted to specific CER topics, including methodology, randomized controlled trials, health technology assessments, and intervention side effects.<sup>41</sup> The objective is to streamline the flow of data and chronicle information available by condition. The Tufts-New England Medical Center's Cost-Effectiveness Analysis Registry provides another prominent example.<sup>42</sup> The registry provides information on cost-utility analyses that reflect quality of life and added life years from treatments. It includes pre-screened, published research in a database that can be searched based on the method of analysis, the target population, type of intervention, comparator treatment, cost-effectiveness ratio, and other criteria.

While not involving CER per se, there also are numerous and growing examples of private sector initiatives to provide healthcare information to patients, especially considering the quality of care. These initiatives illustrate the potential for using information technology to provide healthcare information to patients, employers, and/or providers. A few examples include the Leapfrog Group, formed by a group of large employers in 2000, which provides free online hospital safety ratings by hospital, city, zip code, or state.<sup>43</sup> Consumer Reports rates hospitals by state; HealthGrades provides a searchable database of doctors, hospitals, and nursing homes across the country; and Consumer Health Ratings.com allows individuals to search for organizations that provide free or fee-based ratings of providers and services.<sup>44</sup> WebMD provides numerous types of information about symptoms, conditions, and treatments.<sup>45</sup> The Mayo Clinic provides online information on diseases and conditions, as well as information from "more than 3,300 physicians, scientists and researchers from Mayo" to help patients understand their disease or condition.<sup>46</sup> In addition, major health insurers provide online information on plan costs, general health

information, and physician locations, and some plans provide enrollees with information related to specific diseases (symptoms, treatments, etc.).

#### **IV. Comparative Effectiveness and Cost Effectiveness in other Countries**

CER is employed in many developed countries, generally in the context of more extensive government financing, regulation, or provision of medical care than in the U.S. Important examples that may help inform U.S. policy include Canada, Australia, the U.K., and Germany, especially if pressure mounts for using CER and/or cost effectiveness analysis in coverage decisions. Much of the relevant experience in these countries focuses on the use of CER and cost effectiveness analysis to determine whether the government will pay or otherwise permit coverage of new prescription drugs, medical devices, or medical technology. Each country employs a centralized, government approach. Perceived advantages of centralization compared with decentralized decisions at local government levels include greater consistency and perceived credibility, as well as less duplication of cost.<sup>47</sup>

##### *Examples*

**Canada.** Canada provides health care coverage to all Canadians via a publicly financed system that contracts with private medical care providers. A centralized review process plays an important role in determination of what treatments are funded. While most medical technologies are also subject to review, the focus of the government's efforts is on pharmaceuticals (and biologics). The Canadian Common Drug Review (CDR) reviews the effectiveness, price, and cost-effectiveness of new drugs and makes recommendations to the provinces regarding whether or not to list the drugs on their formularies. CDR staff and external experts review the evidence submitted by the pharmaceutical manufacturer, conduct a separate systematic review, and submit all of the results to the Canadian Expert Drug Advisory Committee (CEDAC). CEDAC, composed of clinicians, reviews all evidence and issues recommendation to the provinces. There are generally three types of recommendations: list, list with restrictions, and do not list.<sup>48</sup>

Based on CEDAC's recommendation, the provincial drug plans are free to make their own decisions on whether and how to list the drug based on the CEDAC review and local priorities and resources. One review of the provincial responses to CEDAC recommendations found differences among provinces in the time taken to respond and the specific responses to CEDAD recommendations, if any, but most decisions that were made appeared to follow the CEDAC recommendation.<sup>49</sup> More recent findings suggest that drug plans take the committee's recommendation in full about 90 percent of the time.<sup>50</sup>

CEDAC transparently posts its recommendations and rationales on a public web site. The recommendations generally reflect the drug's comparative effectiveness, price (over which the committee has no control), and cost-effectiveness. It appears that the committee often has difficulty accepting the results of cost-effectiveness analyses: most of its recommendations criticize those analyses.<sup>51</sup> Comparative effectiveness and price would appear to have much greater influence on recommendations than cost-effectiveness analyses.

**Australia.** Australia provides coverage for pharmaceuticals for all Australians under the Pharmaceutical Benefits Scheme (PBS).<sup>52</sup> In order to be approved for listing, pharmaceuticals must meet comparative effectiveness, cost-effectiveness, and safety criteria. A new drug must be at least as effective as a comparable drug that has already been listed in the same therapeutic class, and it must be at least as cost-effective as that drug. The requirements place a significant burden of proof on the manufacturer to show that the new drug is at least as good as previously listed drugs. When assessing whether a drug meets the criteria, the Pharmaceutical Benefits Advisory Committee (PBAC) considers the price and attendant evidence on cost-effectiveness for the proposed indication submitted by the manufacturer compared to a "designated comparator." The PBAC does not establish the price for the drug, which is determined by a separate committee based on several criteria, including "comments on clinical and cost-effectiveness" from PBAC. The evidence is then reviewed by the health department, consultants, and the PBAC.

The PBAC must issue a positive recommendation for the drug to be listed on the PBS formulary. Its recommendation can allow or specify that specific sub-populations have covered access to the drug or require doctors to obtain permission before prescribing the drug. Negative recommendations can result in resubmission by the manufacturer, which can lower the price, provide additional evidence as to effectiveness, or narrow the indication(s) for which it seeks coverage. Factors affecting the likelihood of reimbursement include the strength of evidence for the comparative effectiveness or cost-effectiveness. If the evidence is strong, the PBAC is likely to recommend coverage if the cost per QALY is acceptable. If the cost per QALY is not acceptable, it may still recommend the drug, especially if the condition is life-threatening.<sup>53</sup> There is some evidence of variation in approvals above and below specific cost per life-year thresholds suggesting a range of cost per life-year thresholds that is acceptable to the committee.<sup>54</sup>

**The United Kingdom.** British citizens receive healthcare coverage through single payer, government funded systems. The National Institute for Health and Clinical Excellence (NICE) has provided guidelines for health care delivery in England and Wales since 1999; it has functioned more in of an advisory capacity in Scotland.<sup>55</sup> NICE sets standards for the use of health technology including



pharmaceuticals, clinical practice, and prevention efforts.<sup>56</sup> NICE guidance on technologies and pharmaceuticals is mandatory, whereas health and clinical guidelines are advisory.

The Department of Health determines the agenda for NICE and submits specific technologies for its review. Stakeholders in the process must formally register as interested parties and are consulted before the final decision is made. In addition to the manufacturer submitting the technology for review, other interested parties may include organizations representing patients, caregivers, and medical professionals. The process begins with the development of a formal statement of the review's intended scope. Once the review's focus has been established, an independent expert panel conducts a meta-analysis of the literature on the technology. Registered stakeholders can submit information and resources and provide feedback on a draft version of the panel's findings. The panel's final report is submitted to an appraisal committee, with a subsequent hearing to receive additional comments from registered stakeholders, testimony from other patient and medical professional groups, and any additional expert testimony. The appraisal committee's assessment is then submitted to NICE for review. NICE formally approves a final guideline and submits it to the National Health Service, which has final authority to approve or disapprove coverage. If NICE and the National Health Service reject a treatment as cost ineffective, patients who want access to the technology must pay for it.<sup>57</sup>

NICE assesses the cost-effectiveness of new treatments compared to the next best treatment currently in use. QALYs are used to measure the health benefits. NICE tends to view interventions as cost effective when the incremental cost-effectiveness ratio is less than £20,000 to £30,000 per QALY. This benchmark is not strict. For conditions with limited treatment options, NICE may accept a higher cost-effectiveness ratio.<sup>58</sup> Research indicates that NICE decisions reflect perceptions of disease burden in addition to cost-effectiveness.<sup>59</sup>

The target QALY threshold is NICE's largest source of criticism from patients, providers, and manufacturers who assert that application of the threshold can produce decisions that fail to serve the interests of patients. Critics also argue that the length of time taken to review a technology is too long and can delay life-saving technology. During 2009-2010, NICE rejected based on cost-ineffectiveness several cancer drugs for indications approved in the U.S., including erlotinib (Tarceva) for non-small cell lung cancer, sorafenib (Nexavar) for advanced hepatocellular carcinoma, and lapatinib (Tykerb) in combination with capecitabine (Xeloda) for advanced or metastatic *HER2*-positive breast cancer.<sup>60</sup>

**Germany.** In 2004, lobbying efforts of sickness funds and physician organizations in Germany resulted in the creation of the Institute for Quality and Economic Efficiency in Health Care (Institut fuer Qualitaet und Wirtschaftlichkeit im Gesundheitswesen or IQWiG). The IQWiG is charged with making decisions about technology to improve economic efficiency in health care delivery.<sup>61</sup> The IQWiG's

agenda is determined jointly by the Ministry of Health and the national committee of physicians and health insurance funds (Gemeinsamer Bundesausschuss or G-BA).

The review process begins with publication of the evaluation criteria for a specific technology. The IQWiG's initial review is based a select subset of evidence, and the criteria are not consistent across assessments. The IQWiG typically restricts acceptable evidence to published head-to-head trials against technologies already registered in Germany. Evaluation of clinical effects is based on reported complications, mortality, and morbidity from randomized controlled trials. Additionally, the IQWiG may directly consult manufacturers or elicit external expert opinion. The IQWiG also determines a recommended ceiling price at which a health technology deemed as superior in a therapeutic area should be reimbursed.

Following review of the evidence, the IQWiG publicly distributes an initial report for formal comment (within a month) by manufacturers and other concerned parties (with a six page limit). A hearing may follow in which testimony from patients and other experts can be obtained. Following a final review, the IQWiG's report is submitted to the G-BA, which is ultimately responsible for coverage decisions. The G-BA may consider additional evidence previously excluded by IQWiG.

The IQWiG's review is not based on cost-effectiveness analysis or economic modeling. One of the main criticisms of the IQWiG is the lack of an explicit statement of assessment criteria. Efforts have been undertaken by the IQWiG to improve transparency about the methodological approach. A second criticism of the IQWiG's health technology assessment is that it allows insufficient participation by manufacturers and other interested parties, although limited input of those parties prior to the final IQWiG report is partially offset by the more political and open process once the final support is submitted to the G-BA.

### *Transparency*

An important issue in government reviews and approvals of medical treatments is the transparency of the review process and rationales for decisions.<sup>62</sup> Canada's CDR posts its recommendations and the rationale behind those recommendations on a public web site. Australia has undergone a gradual and successful transition to a transparent process. Although the PBAC formerly did not provide rationales for its recommendations due to privacy concerns, demand for increased transparency has led the agency to publish explanations of its underlying decision online.<sup>63</sup> The NICE review process is characterized by a high level of transparency and external participation. The formal processes of registering interested parties and providing opportunities for input, even in the earliest stages of developing a review's scope, provide a transparent forum for evaluation. The "full details of its guidance, including the reasoning

behinds [NICE's] recommendations" are available to the public.<sup>64</sup> While the review process has been criticized as onerous and long, the commitment to transparency and dialogue is viewed positively.

In Germany, evidence is restricted to direct comparison from randomized controlled trials in the first stages of the review process. External experts involved in the review are not identified to interested parties. Communication with interested parties, especially manufacturers, is often highly constrained. Assessments by the G-BA are transparent in terms of procedural rules and the criteria used to make assessments, but the bases for final decisions are not clearly outlined for the public.<sup>65</sup> The lack of transparency and restricted dialogue with manufacturers are considered problematic.

## **V. Greater Public Investment in CER: the Right Path for the U.S.?**

The preceding background illustrates the complex, difficult, and bureaucratic issues that need to be addressed in any system of government funding and administration of CER. A more basic policy choice confronting the U.S. is the relative roles of public vs. private sector investment and involvement in CER. The development of economically efficient policy towards CER must address at least two fundamental questions. The first question is the extent to which underprovision of CER in the private sector justifies substantial public subsidies. The second question involves the assessment of the best approaches to subsidizing CER.

The most common argument for significant public investment in CER in the U.S. is that the private sector significantly underprovides CER as evidenced by: (1) the negligible amounts of private sector spending on CER in relation to total health spending, (2) significant regional variation in Medicare and perhaps other healthcare spending that has not been readily explained by differences in the need for and quality of care, and (3) statements by the IOM and others that less than half of all medical treatments are supported by evidence. The primary blame for inadequate private sector CER is generally placed on the public good nature of investments in information. Significant public funding is viewed as the appropriate remedy given public financing of Medicare and Medicaid, perceived economies of scale and scope in conducting CER, historical involvement of the federal government in funding health and other forms of research, and a belief that government approval / oversight of CER that is funded is required to ensure that the methods and results of CER are objective, credible, and appropriately prioritized.

### *The Dearth of Evidence-Based Medicine*

While total private spending on CER is difficult to estimate accurately, the consensus that such spending represents a very small fraction of total healthcare spending is certainly correct. The evidence and implications of regional variation in healthcare spending, most of which is for Medicare spending, are less clear cut. Regional Medicare spending clearly varies significantly after controlling for differences in

local wages and prices and broad demographic characteristics of the population. It is also clear that this variation is associated with differences in the number and intensity of services provided. Evidence is less definitive on the extent to which higher than average spending does little or nothing to increase quality of care, or is not in significant part attributable to differences in underlying population health.<sup>66</sup>

Some evidence, for example, suggests that higher end of life spending is associated with lower hospital mortality rates for certain conditions.<sup>67</sup> The possibility exists that the regional variation literature overstates the amount of variation, perhaps significantly, that is not associated with differences in quality and health status. While additional research will help clarify these issues, the claim that up to 30 percent of Medicare spending could be eliminated without a non-trivial reduction in the quality of care and health outcomes could be highly optimistic.

Assessments by the IOM and others that less than half of medical decisions are based on evidence have provided support for increased government funding (or other subsidies) to CER. The quantitative if not qualitative validity of such assessments, however, depends at least in part on the definition of “evidence.” If the term is restricted to systematic quantitative assessments involving clinical trials or well-designed observational studies, then such assessments are likely valid. Defining evidence to encompass the diffuse knowledge obtained by hundreds of thousands of physicians from treating individual patients over time through custom and practice would almost certainly produce a much higher figure for the proportion of medical treatment that is “evidence-based.”

#### *CER as a Quasi-Public Good vs. Perverse Payment System Incentives*

In general, the degree to which private investment in CER is socially inadequate depends on the cost of generating the research and the ability or inability to charge users for the information. Private investment will be forthcoming as long as the expected value created by the investment, in terms of the willingness of consumers to pay, exceeds the cost of investment and the investing entity can charge for the good or service. Private entities will invest when they are able to charge enough for the good or service to justify the cost of investment.

As noted above, the conventional argument for increased public spending on CER is that it constitutes a “public good” that will be underprovided by the private sector. This public good (or quasi-public good) rationale for public subsidies to CER has two main tenets. First, once evidence is generated following a significant investment in CER, the marginal cost of making it broadly available is negligible and much lower than the marginal benefits. Second, it would generally be too costly or even infeasible for a private creator of such evidence to exclude users who do not pay for the information. The upshot is that private players will generally find it uneconomical to invest in CER that has a large social benefit, or,

if they could charge enough for access to the findings to justify the upfront investment, many potential users would value the information more than its marginal cost but less than the price charged, sacrificing potential welfare gains.

Conventional economic analysis of public goods favors public subsidies to the provision of “pure” public goods (zero marginal cost and complete inability to exclude non-payers). For quasi-public goods, where production requires high fixed costs, the marginal cost of additional supply is small, and some degree of excludability is feasible, the case for public subsidies is less certain. An alternative and widely used tool to promote supply under those conditions is to provide intellectual property rights through patent, copyright, and trademark law. The general assumption in the CER debate has been that intellectual property rights do not prevent substantial underinvestment in CER in the private sector.

The costs of undertaking CER can be large, especially if randomized clinical trials are involved. The results of such research, however, are not inherently non-excludable for non-payers. There exist dozens of examples of firms that collect, analyze, and synthesize data while limiting access to entities that pay the firms substantial fees for access to the information, including numerous firms that specialize in healthcare. While the existence of these arrangements does not imply that expanded public support of CER would not be efficient, it does undermine the public goods rationale for such support.

Indeed, a strong argument can be made that the public good argument for significant increases in public investment in CER has received attention that is disproportionate to its merit, and that the U.S. system of public and private insurance is a far more important disincentive for private sector CER than any public goods problem.<sup>68</sup> It is hardly surprising that private players’ incentives for investments in CER related to medical spending for Medicare enrollees are weak, given that official Medicare payment policy has for the most part carefully avoided making payment decisions based on comparative effectiveness. Moreover, both Medicare and private health insurance are widely recognized as contributing to substantial moral hazard and excessive utilization of low-valued medical care.

The well-known consensus among economists is that the tax exclusion of employer contributions for workers’ health coverage (and, with appropriate design, workers’ contributions) encourages workers and their families, especially those with higher incomes, to choose generous coverage.<sup>69</sup> That tax-induced increase in coverage produces extensive moral hazard and excessive utilization of low-valued medical care, including less willingness to choose tighter managed care arrangements with limits on access to specialists and other high cost care. Moreover, the traditional Medicare program, which covers 75 percent of enrollees, provides fee-for-service coverage without managed care restrictions.<sup>70</sup> A large majority of enrollees obtain supplement coverage for most Medicare cost-sharing through individually

purchased or employer-sponsored supplementary coverage. These coverage arrangements likewise contribute to the demand and supply of low-valued care in traditional Medicare.

While not directly comparing costs of treatments, a major function of CER is to provide information that can be considered by physicians and patients, along with information on costs, when deciding on a course of treatment. Because the insurance system significantly insulates patients and providers from costs, it reduces the demand for CER that could shed light on the relative benefits of different treatments, including what constitutes low-value care. If patients and their physicians had more incentive to consider costs, there would be a correspondingly greater demand for information on comparative effectiveness to guide their decisions.<sup>71</sup>

In short, the tax/insurance system reduces the value to patients and providers of information from CER. Changes in the tax/insurance system to reduce moral hazard would reduce excessive utilization of low-value care and increase the demand for information to help identify such care.

#### *The Strengths and Weaknesses of Public Funding*

Public funding is one tool for promoting CER. Policy changes that would increase incentives for patients and providers to demand more information to guide decisions would substantially increase the flow of private sector CER, reducing the case for expanded public funding. If such changes are infeasible, the case for greater public funding is strengthened, even though the public good rationale does not imply that public funding would necessarily be superior to other forms of subsidizing CER, such as expanded and refundable tax credits.

Public funding of CER requires a system of allocating the amount of funds appropriated by Congress among research areas, specific projects, and investments in infrastructure to spur CER. Important issues include the location of administrative authority (e.g., within an existing agency, creation of a new agency, etc.) and specific procedures for attempting to ensure that allocation decisions achieve program objectives in an unbiased, credible, and transparent fashion.

The history of public funding of medical and other scientific research, including through the NIH and AHRQ, provides lessons and guidance for the design of public funding of CER in the U.S. and contributes to the belief by many observers that a well-designed system for funding CER can effectively allocate limited funds based on suitable priorities, expertise, and research capabilities.<sup>72</sup> Thousands of medical care researchers and hundreds of institutions already have infrastructure and experience with seeking and obtaining federal grants, with well-established review criteria.

Many observers regard substantial public funding of CER as inherently preferable to private sector investment, even apart from the scope of the public goods problem or dearth of investment due to the

chilling effects of the payment system. Some have a strong preference for universal health insurance with little cost-sharing, which favors increased government control over medical decisions to limit cost growth. Some believe that only the government is able to provide and allocate sufficient funds to meet perceived needs for CER. More broadly, many observers regard public allocation of CER funding as essential to ensure that funded research is correctly prioritized in view of society's needs and is objective, credible, coordinated, and of high quality.

Whatever the strength of those arguments, there are inherent limitations to public funding of CER. At a basic level, public funding of CER necessarily involves a form of “winner picking,” which runs up against widely held views that the government should generally avoid directing funds to specific investment projects, as opposed to improving incentives for decentralized, private investment. Apart from this basic philosophical objection, most observers would agree that public funding of CER confronts two broad problems, and that the best achievable results will necessarily be far from perfect. The problems are: (1) how to prioritize and allocate funds to add the most value in the face of substantial complexity, uncertainty, and pressure from special interests; and (2) how to deal with patient heterogeneity so as to minimize unintended consequences. Increased public funding of CER also involves an inherent risk of crowding out (future) private investment, both directly and indirectly through its potential effects on payment system reforms. It also could increase pressure for extending public investment and decision-making to encompass cost-effectiveness, and for using the results of CER and cost-effectiveness decisions to make coverage and reimbursement decisions, moving the U.S. toward much greater government control of healthcare.

**Prioritization / Allocation.** Human conditions that might benefit from medical care, the volume and scope of alternative treatments, variation in responses among patients to treatments, uncertainty about the effects of treatments, and the dynamic evolution of knowledge are enormously complex. This complexity and uncertainty poses daunting challenges for centralized, publicly funded systems for CER. From a normative, economic perspective, public prioritization / allocation decisions for CER should maximize the net benefits of investment as guided by the potential value of information from specific forms of research. Specifically, decisions should seek to allocate limited funds to maximize expected net benefits from improving health within a “value of information” (VOI) framework, and the organization and administration of public funding of CER should be designed to achieve that goal.<sup>73</sup>

Whether formally or informally, applying the VOI framework requires consideration of the value of health outcomes based on a summary measure of health outcomes, such as a QALY. Alternative modes of treatment or intervention must be identified, and the potential findings and timeliness of the

research results must be evaluated. Prioritization / allocation decisions also should consider the likelihood that the research findings will change clinical decisions.

It generally is agreed that public prioritization / allocation decisions should reflect broad expertise and public input, and that the decision making process and structure should try to minimize conflicts of interest. Even with the best intentions and design, however, interest groups and rent seeking behavior will impact decisions, and rent seeking will engender significant costs in lobbying expenses and other expenditures to influence prioritization and the amounts and impacts of CER finding. Small, organized groups with high financial and/or intellectual stakes in the outcomes of the decisions will inevitably exert disproportionate influence.<sup>74</sup>

The results and process of the IOM's ranking of priorities in response to the ARRA illustrates the issues and difficulties involved in prioritizing CER.<sup>75</sup> The IOM's charge was to develop a list of high priority questions for CER. The organization solicited input from more than 20,000 individuals and organizations and received input from direct mail, a web-based questionnaire, and a public session with "54 individuals representing consumers, patient advocacy groups, provider groups, insurers, manufacturers, and academia," and a web-based questionnaire that "requested nominations, was open for 3 weeks, and received 1,758 submissions of more than 2,600 topics." Based on three rounds of voting, an IOM committee identified 100 top priority areas for CER in 29 research areas "affecting a broad range of age and ethnicity," with 24 areas affecting "special populations."

The 100 research topics were divided into priority quartiles. Examples from the first (highest priority) quartile include (the IOM report summary does not provide rankings within quartile) treatments or interventions for hearing loss, tooth decay, and unintended pregnancy:

- Compare the effectiveness of the different treatments (e.g., assistive listening devices, cochlear implants, electric-acoustic devices, habilitation and rehabilitation methods [auditory/oral, sign language, and total communication]) for hearing loss in children and adults, especially individuals with diverse cultural, language, medical, and developmental backgrounds.
- Compare the effectiveness of the various delivery models (e.g., primary care, dental offices, schools, mobile vans) in preventing dental caries (tooth decay) in children.
- Compare the effectiveness of innovative strategies for preventing unintended pregnancies (e.g., over-the-counter access to oral contraceptives or other hormonal methods, expanding access to long-acting methods for young women, providing free contraceptive methods at public clinics, pharmacies, or other locations).

Examples from the lowest priority quartile include heart disease imaging, pharmacologic disease management, and back surgery:



- Compare the effectiveness of computed tomography (CT) angiography and conventional angiography in assessing coronary stenosis in patients at moderate pretest risk of coronary artery disease.
- Compare the effectiveness of different disease management strategies in improving the adherence to and value of pharmacologic treatments for the elderly.
- Compare the effectiveness (e.g., pain relief, functional outcomes) of different surgical strategies for symptomatic cervical disc herniation in patients for whom appropriate nonsurgical care has failed.

A non-expert might question the rationale for such rankings. More generally, although the IOM's guidelines for rankings considered factors that would be important in a VOI analysis, such rankings are likely to be only roughly related to the expected economic value added by CER on different interventions.

**Timeliness and Value of Findings.** Even with the best design, research by its nature involves substantial uncertainty about the value of findings. It is likely that a non-trivial amount of publicly funded CER would have little impact on care decisions even if patients and providers were incentivized to consider the results. The reason is that much research will be non-informative – it will not provide clear evidence of the differential effects of treatments. In the world of academic research, inconclusive results can be difficult to publish. In a world of publicly funded CER, inconclusive results will not affect outcomes. The problem of inconclusive (or unconvincing) results is especially likely for many observational studies, where questions of causality will arise regardless of the care in which the research was conducted.

As discussed in section II, the types of research that would be necessary to compare many forms of treatment also will involve substantial time and delay, in addition to effort and resources. In a dynamic environment of medical research and practice, some research will be dated by the time that the results are obtained, as new treatments are approved and introduced. The unavoidable bureaucracy involved in prioritizing research areas, approving specific projects, and reviewing the results of those projects is likely to make this problem more severe for publicly funded CER than would be true for decentralized, privately funded research, or at least to reduce the advantages of public funding.

**Heterogeneity in Patient Responses.** Heterogeneity in patient responses to treatments also represents a formidable obstacle to improving health outcomes efficiently through public funding of CER. When patients respond differently to different treatments, a treatment that achieves the best results for a majority of patients may produce distinctly inferior results for other patients. In recognition of this problem, many observers stress the importance of considering the possible effects of treatments on subgroups of patients in a system of publicly funded CER. This is easier said than done, as heterogeneity

in responses significantly complicates the prioritization problem and the design of research that is likely to generate informative findings.

Assuming that physicians pay attention to the findings, results suggesting that a particular treatment is superior on average may increase physicians' focus on that treatment even though alternative treatments might be preferable for subgroups of patients. This problem will be exacerbated to the extent that the results of CER were to affect reimbursement decisions, including the possibility that heterogeneity in patient responses could cause the results of CER to reduce total health by discouraging the use of treatments that would benefit some patients.<sup>76</sup>

**Direct and Indirect Crowd Out.** While the supply of CER by the private sector is small in relation to health spending, it is growing and far from zero in absolute terms. Apart from the theoretical realm of pure public goods, any significant amount of public investment will directly crowd out some investment by private players such as health insurers, managed care organizations, and research foundations, thus reducing the net benefits of public investment. While the amount of potential crowd out might be perceived as small based on current private sector efforts, the development of public funding mechanisms for CER will lead to some reduction in incentives for possible future investment in CER by private entities.

There also exists a risk of indirect crowd out of private sector investment from expansion of public sector CER. The desire to reduce spending on low-valued medical care is a significant impetus for public funding of CER. A major public investment in CER might soften pressure for market-oriented reforms that would provide stronger financial incentives (as opposed to stronger controls over physician reimbursement) for patients and physicians to eschew low-valued care. A failure to strengthen those incentives over time will generate greater cost and budget pressure, with commensurate increases in demands for public funding of CER, for expanding public research funding to emphasize cost effectiveness, and for greater use of CER and cost effectiveness analyses in coverage and reimbursement decisions.

## **VI. Promoting Private Sector CER**

The passage of the healthcare reform law notwithstanding, projected growth rates for U.S. government and private healthcare spending are unsustainable. Sooner or later, additional government and private sector actions will necessarily be taken to achieve sustainability. Divergent approaches to achieving sustainability range from progressively increasing government control over insurance reimbursement, provider reimbursement, and the types of care provided to adopting incentive-based, consumer-driven policies that rely on patient preferences and competition.

Increased public investment in CER by itself will likely have only a modest impact on achieving sustainability. Without significant changes in incentives provided by public and private insurance, publicly funded CER will likely produce some increase in the utilization of medical treatments that are shown to be superior in CER and some decrease in utilization of treatments that are less effective. Depending on the specific research results and the effects of patient heterogeneity, the overall quality of care could marginally increase, and, more optimistically, there could be some reduction in expenditures. More substantive effects from public funding of CER would require patients, providers, and insurers' decisions to pay closer attention to both the costs and comparative effectiveness of different treatments. That in turn would require establishment of greater linkage between CER results and public / private insurance reimbursement and/or changes in consumer / physician incentives for utilization of low-value, high cost treatments.

#### *Incentivizing Demand for CER*

Increases in the cost of private health insurance have resulted in greater attention being paid to costs by employers, employees (who face more cost-sharing and higher premium contributions), individual insurance purchasers (with high deductible plans and/or tax-advantaged health savings plans), and insurers. That trend will likely continue absent contradictory policy changes, and it should be accompanied by growing demand for information about what treatments work best and the costs of different treatments.

While public investment of CER has certain advantages, its inherent limitations favor policies that seek to promote and expand the supply of information in the private sector, including increased private sector CER, to reduce or complement public CER. The most powerful tool for increasing private sector CER would be to adopt policies that increase incentives for patients and healthcare providers to pay closer attention to both the costs and benefits of care. There exist two broad policy options for achieving that goal: (1) reducing the tax subsidy to generous health insurance, and (2) modernizing Medicare to promote enrollee choice.

**Reducing the Tax Subsidy for Generous Health Insurance.** A large majority of economists conclude that incentives for considering the costs as well as benefits of medical care could be increased in the private sector by reducing the tax subsidy to employer-sponsored health insurance (and by changing tax rules to help achieve tax neutrality between employer-sponsored and individual health insurance). Appropriate policy on this dimension would encourage a shift away from health plans that essentially provide pre-paid health care toward health plans that focus instead on providing insurance protection against large and potentially catastrophic expenses. It also would reduce the incentives for employees to obtain coverage from health plans with relatively little management of care, with the result that more

employers and employees would choose plans with effective management of care to limit excessive utilization, even though such plans limit patients' choices for certain types of care.

The PPACA's provision imposing a 40 percent tax on very high cost health plans beginning in 2018 represents a modest step in reducing the tax subsidy to generous health plans. Numerous proposals that would have much more bite have been made, including replacement of the current tax exclusion for employer-sponsored health coverage with a limited system of refundable tax credits. The key point in the context of public and private funding of CER is that further reductions in the tax subsidy for private health insurance would significantly increase the demand for information about the benefits and costs of medical treatment, including information that could be provided by expanded private sector CER. It would also increase incentives for cost-effective innovation.

**Modernizing Medicare to Promote Enrollee Choice.** Improving incentives for Medicare enrollees and providers to pay closer attention to the costs as well as benefits of different treatments could be achieved by changes that move away from the traditional program's fee-for-service payment with unlimited choice of providers. The PPACA's provisions enabling the formation of physician-based accountable care organizations represent a step towards increasing providers' incentives to pay closer attention to utilization.<sup>77</sup> On the other hand, the PPACA's cuts in reimbursement for private Medicare managed care plans (Medicare Advantage) will reduce their growth and result in more enrollees being covered by fee-for-service Medicare, and the PPACA's large proposed cuts in provider reimbursement by Medicare may presage future developments absent fundamental changes to improve incentives.

A variety of proposals have been made for changing the design of Medicare (with long transition periods) to increase incentives for enrollees and providers to pay closer attention to the costs and benefits of different treatments. Two broad and related approaches include: (1) allowing Medicare enrollees choice among plans with different levels of cost sharing and premiums, and (2) transforming Medicare to a premium support (defined contribution) system where enrollees receive specified dollar premium subsidies to select among alternative private plans.<sup>78</sup> While both proposals are controversial, the key point here is that moving in either direction would substantially increase the demand for information about the benefits and costs of different medical treatments, including CER, and it would also increase incentives for cost-effective innovation.

### *Responses to Increased Demand*

The increase in the demand for information in general and CER in particular that would flow from changes in the tax/insurance system to incentivize patients and providers to pay closer attention to costs and benefits of medical care would increase incentives for private entities to supply information,

including CER, reducing the need for or desirability of expanded public investment in CER. Developers of new treatments and technologies, providers, and other private entities would have stronger incentives to produce information about quality, comparative effectiveness, and cost-effectiveness to guide medical care decisions.

Increases in the demand for information would accelerate private sector initiatives to meet that demand and reduce the effects of free rider problems that in theory could make such investment unattractive. In particular, increased demand for information about comparative effectiveness would likely create a large potential for increases in investment to establish and market cost-effective treatment protocols. Some innovations in treatment protocols would likely be protectable as intellectual property, thus allowing for patents and licensing. Perhaps more important, increased demand for information on the effectiveness of treatments would create greater opportunities for branding, licensing, and certifying efficient treatment protocols that are not patentable, which in turn would encourage investment in research to aid the development and maintenance of such protocols.

To elaborate on the types of innovation that would be encouraged, a number of U.S. health systems currently have established reputations for high quality and efficient care. They are often offered as models by observers who emphasize potential wasteful spending on health care. Increases in the demand for cost-effective care and information about providers that provide such care would encourage additional providers to adopt such models. It also would create the potential for high-reputation health systems to develop and license brand names and trademarks (e.g., the “Mayo Method,” the “Geisinger Approach,” or the “Penn Protocol”) to entities that adopt and comply with their processes and procedures. Similarly, innovators in the development of cost-effective treatments would have the potential ability to brand and market their trademarks as indicators of adoption and quality.

Increases in the demand for information about cost-effective medical care would also expand market opportunities for the development of ratings and certification systems, where private rating agencies would rate or certify the performance of health systems and other providers in terms of their quality and efficiency. The byproduct again would be increased demand for and funding of research to identify, evaluate, assess, and certify effective modes of care. More generally, the overall environment engendered by increased demand for information about cost effectiveness would stimulate significant innovation to capture value from meeting that demand.

#### *Lowering the Cost of CER*

Without major policy changes to increase incentives for patients and providers to consider effectiveness and costs of care, or until such changes are adopted, increases in the cost of medical care

and insurance and growing cost sharing in employer-sponsored and individual health insurance plans (to the extent allowed by the PPACA) should continue to increase the demand for and supply of information about comparative effectiveness. This trend simultaneously weakens the positive case for additional public investment in CER and increases the risk of crowd out from such investment.

Additional strategies for promoting the supply of CER in the private sector include possible adoption of policies to lower the cost of CER. Expanded tax subsidies to private CER could substitute for or complement public funding. Private investment in CER that qualifies as “research and development” (R&D) under the U.S. tax code is already deductible for tax purposes in the year expenses are incurred, and it might qualify for existing R&D tax credits. Expenditures for some types of CER may qualify for R&D tax credits. Consideration could be given to providing broader and/or additional, designated tax credits for research expenditures that meet enumerated criteria for CER. To further expand incentives, the credits might be made refundable (grants) for non-profit and other non-tax paying institutions. Compared with public funding, prioritization, and selection of CER projects, increased tax subsidies, a method of partially matching private funds with public dollars, would lever taxpayer investment. It also would permit decentralized, private decisions about areas for CER that are perceived as having the greatest potential to add value, as opposed to relying on prioritization and selection of projects by a government or quasi-government agency.

Decentralized CER tax subsidies would raise the issue of possibly greater bias and less credibility of the findings of some subsidized CER than would be the case with direct public funding. However, the direct users of the CER results would still be insurers, health systems and other providers, and researchers with substantial ability and expertise for assessing the value and credibility of CER. There are a number of precedents for sector-specific R&D tax credits, including in healthcare. Notably, the PPACA provides \$1 billion targeted to small biotech, pharmaceutical, and medical device companies (less than 250 employees) in the form of tax credits or grants equal to 50 percent of investment incurred in 2009-2010 for qualified biomedical research. The Internal Revenue Service describes the program as follows: “The credit will be allocated among projects that show significant potential to produce new and cost-saving therapies, support good jobs, and increase U.S. competitiveness.”<sup>79</sup>

The PPACA also includes in its CER provisions a charge for the PCORI to expand the availability of medical claims and related data for use in conducting CER as a means to encourage research using those data by PCORI-funded researchers that enter into data agreements with the PCORI or other government agencies. Public investment in additional data and making existing data accessible for research represent relatively low costs methods of encouraging CER, and there is scope for action that goes beyond the PPACA’s provisions.

Concerns about privacy of medical data and associated restrictions on data availability pose barriers to CER that might be reduced by revising regulations and legal rules in ways that could better promote CER.<sup>80</sup> Moreover, obtaining access to medical claims and related data and entering into and administering data agreements with government agencies involves fixed costs that likely discourage a sizable amount of observational research that would have the potential to provide valuable information on comparative effectiveness. Medical and health services researchers at medical schools, university departments of public health, and non-academic research institutes generally rely primarily on external grants for funding, especially from government, including for paying a large proportion of compensation to researchers and support staff. These entities' operations achieve returns to scale in grant writing and interacting with government agencies that support research. There are also large numbers of academic researchers (e.g., economists, statisticians, operations researchers) in colleges of arts and sciences and business schools with expertise in conducting scientifically rigorous observational studies. Many spend a substantial proportion of their time conducting unfunded (non-grant) research for publication in scholarly journals. The availability of and ease of using data has a major impact on their research agendas. Initiatives to make medical claims and related data more widely accessible to researchers, without pre-approval by a government agency of the research topic, would likely cause many additional researchers to allocate effort to CER and related research, without requiring direct government funding of their time and research support.

## **VII. Conclusions**

Increases in CER may have the potential to reduce the growth rate in U.S. healthcare spending – while improving the overall quality of care. Proposals for increased public spending on CER have generated controversy and concern that government-sponsored CER would ultimately be used to make coverage decisions under Medicare and/or private insurance and evolve to encompass cost effectiveness. Regardless of the force of such concerns, the complexity and dynamism of modern healthcare and the inherent limitations of public investment make it desirable to encourage substantial and diverse private sector investment in CER. Well-designed policies to increase incentives for private sector CER have the potential to increase significantly the evidentiary basis of medical decisions, including the stimulation of entrepreneurial investment to guide such decisions.

Although the public good characteristics of investment in information reduce private incentives for investment in CER, the reduction in demand for such research attributable to the design of government and private health insurance and associated provider reimbursement represents a greater impediment. Changes in insurance and reimbursement system design that would incentivize employers, patients, and providers to pay closer attention to the costs as well as benefits of care would increase the demand for and

supply of CER in the private sector. Even apart from the disincentives for CER from the insurance system, careful attention should be paid to policies for subsidizing CER without direct government funding and allocation of CER funds. Particular attention should be given to promoting the open availability of research data on medical treatments and health outcomes and to the possibility of expanding tax incentives to promote decentralized, private investment in CER.



## Notes

- <sup>1</sup> AcademyHealth (2005); Sisko, et al. (2009). The October 2010 issue of *Health Affairs* is devoted to articles on national strategy, costs, value, data, and methods of CER. Donnelly (2010) provides a brief overview of CER and associated policy issues.
- <sup>2</sup> According to the Medicare Board of Trustees (2010), for example, the estimated present-value of the hospital program deficit and general revenues needed to fund other Medicare benefits over 75 years was close to \$23 billion at year-end 2009, even with clearly unrealistically low assumptions about physician reimbursement.
- <sup>3</sup> IOM (2009), citing McGlynn, et al. (2003) and Mangione-Smith, et al. (2007).
- <sup>4</sup> See Yasaitis, et al. (2009); Fisher, et al. (2003), and Baicker and Chandra (2004).
- <sup>5</sup> See, for example, Cannon (2009).
- <sup>6</sup> CBO (2007) and IOM (2009). Also see Docteur and Berenson (2010).
- <sup>7</sup> CBO (2007) provides a detailed overview. Also see Federal Coordinating Council (2009) and Tunis (2009).
- <sup>8</sup> IOM (2009), Tunis (2009), and Docteur and Berenson (2010).
- <sup>9</sup> IOM (2009).
- <sup>10</sup> Sox, et al. (2009).
- <sup>11</sup> Luce, et al. (2009); Tunis, Stryer, and Clancy (2003)
- <sup>12</sup> Luce, et al. (2008).
- <sup>13</sup> Dreyer, et al. (2010) discuss potential advantages and limitations of observational studies compared with RCTs. Federal Coordinating Council (2009) lists relevant databases and their availability for research.
- <sup>14</sup> Sox, et al. (2009); Dreyer, et al. (2010).
- <sup>15</sup> CBO (2007); Luce, et al. (2008).
- <sup>16</sup> Section IV includes additional discussion of this issue in the context of other countries.
- <sup>17</sup> See Pearson (2009) for an example.
- <sup>18</sup> Cutler (2004) provides basic background and examples of cost effectiveness analysis.
- <sup>19</sup> Jacobson (2007).
- <sup>20</sup> Wilensky (2008, 2009); ACP (2008).
- <sup>21</sup> Tunis (2009) provides an example of the former view and Wilensky (2009) the latter. Garber and Sox (2010) advocate including information and data on cost in the CER that is funded by the Patient Centered Outcomes Research Institute under the PPACA (see below,) without having the research include cost effectiveness analysis, so that others will be able to perform such analyses.
- <sup>22</sup> CBO (2010); CMS Office of the Actuary (2010).
- <sup>23</sup> See, for example, Docteur and Berenson (2010). Basu and Philipson (2010) provide related discussion of the possible effects of CER on demand and spending if CER is used for insurance coverage and reimbursement decisions.
- <sup>24</sup> The Federal Coordinating Council (2009) provides detailed tabulations of prior U.S. government funding of CER through the NIH, AHRQ, and other agencies.
- <sup>25</sup> National Institutes of Health (2010).
- <sup>26</sup> Federal Coordinating Council (2009). Examples of current NIH-funded CER include comparative effectiveness in genomic medicine (University of Pennsylvania); comparative effectiveness of FIT vs. colonoscopy for colon cancer screening (University of Iowa), and comparative analysis of surgical treatment options for localized prostate cancer (Sloan Kettering). <http://deainfo.nci.nih.gov/advisory/ctac/0310/presentations/Croyle.pdf>.
- <sup>27</sup> In addition to healthcare services research, AHRQ conducts data collection, measurement, dissemination, and translation, as well as program evaluation and grant review support (AHRQ, 2010).
- <sup>28</sup> Federal Coordinating Council (2009). Current examples of AHRQ-funded CER include comparative effectiveness of time-adjusted trauma center care on mortality (University of Pennsylvania); comparative safety of anti-retrovirals among HIV-infected patients (UNC Chapel Hill); and the effect of baby friendly health care policies

on breastfeeding (also at UNC Chapel Hill).

[http://gold.ahrq.gov/projectsearch/grant\\_search\\_result.jsp?SORT=YEAR&PORT=A](http://gold.ahrq.gov/projectsearch/grant_search_result.jsp?SORT=YEAR&PORT=A).

<sup>29</sup> Kupersmith (2009). One VA study provided evidence that optimal medical therapy alone was just as effective as a combination of percutaneous coronary intervention plus medical therapy in preventing heart attack and death (Federal Coordinating Council, 2009). Other examples include analyses of resident hours and patient safety (Rosen, et al., 2009) and the effects of improved integration of HIV care (Hoang, et al., 2009).

<sup>30</sup> Saha, Coffman, and Smits (2010).

<sup>31</sup> While Medicare sometimes considers the results of CER in its national coverage decisions (IOM, 2009), Medicare “typically does not reject coverage for a technology that is effective, even if it is less effective than an alternative” (Docteur and Berenson, 2010).

<sup>32</sup> PPACA, Section 1181(a)(2)(B).

<sup>33</sup> AAMC (2010).

<sup>34</sup> PPACA, Section 1182, “Limitations on Certain Uses of Comparative Clinical Effectiveness Research.” Also see Pearson and Bach (2010).

<sup>35</sup> See Federal Coordinating Council (2009) and Blue Cross Blue Shield (2009).

<sup>36</sup> Pearson (2009).

<sup>37</sup> This method for rating the clinical effectiveness is modeled on the “Evidence- Based Medicine (EBM) matrix” developed by America’s Health Insurance Plans (Pearson, 2009). Also see Clancy and Collins (2010) and <http://www.icer-review.org/>.

<sup>38</sup> Hayes (2010).

<sup>39</sup> Emergency Care Research Institute (2010).

<sup>40</sup> [http://www.medgadget.com/archives/2010/06/medicalis\\_releases\\_comparative\\_effectiveness\\_tool\\_for\\_medical\\_imaging.html](http://www.medgadget.com/archives/2010/06/medicalis_releases_comparative_effectiveness_tool_for_medical_imaging.html).

<sup>41</sup> <http://www.thecochranelibrary.com/view/0/AboutTheCochraneLibrary.html>.

<sup>42</sup> <https://research.tufts-nemc.org/cear/Default.aspx>.

<sup>43</sup> <http://www.leapfroggroup.org/cp>.

<sup>44</sup> <http://www.consumerreports.org/health/doctors-hospitals/hospital-ratings.htm>; <http://www.healthgrades.com/>; <http://consumerhealthratings.com/index.php>; [www.webmd.com/](http://www.webmd.com/).

<sup>45</sup> <http://www.webmd.com/>.

<sup>46</sup> <http://www.mayoclinic.com/>.

<sup>47</sup> Hailey (2009) argues that a possible shift towards a more decentralized approach in Australia would “increase regulatory compliance costs, and delay the introduction of new treatments, with adverse impacts on patient outcomes and company revenues.” The Canadian and British systems involve input of local levels of government in the review process (Menon & Stafinski, 2009; Morgan et al., 2006).

<sup>48</sup> There also may be an option, recently added, to list a drug like other drugs in its class (Danzon and Taylor, 2010). Also see Laupacis (2006).

<sup>49</sup> McMahon, Morgan, and Mitton (2006).

<sup>50</sup> Cited in Clement, Harris, Li et al. (2009).

<sup>51</sup> Danzon and Taylor (2010).

<sup>52</sup> Duckett (2004); Henry, Hill and Harris (2005); Harris, et al., (2008); Morgan, McMahon, and Greyson (2008); Chalkidou, et al. (2009); and Hailey (2009) examine various aspects of the Australian system.

<sup>53</sup> Harris, Hill, Chin, et al. (2008); Hailey (2009).

<sup>54</sup> Duckett (2004); Hailey (2009).

<sup>55</sup> See Schlander (2008), Chalkidou, et al. (2009), and Drummond and Sorenson (2009) for additional discussion.

<sup>56</sup> Pharmaceuticals that have not been reviewed by NICE are covered or not based on local decisions.

<sup>57</sup> There is also an appeals process, but it is characterized as restrictive and limited in scope (e.g., Menon and Stafinski, 2009).

- <sup>58</sup> NICE (2008).
- <sup>59</sup> Devlin and Parkin (2004).
- <sup>60</sup> Frandzel (2010).
- <sup>61</sup> See Fricke & Dauben (2009); Perleth, Gibis, and Gohlen (2009); and Sculpher and Claxton (2010) for further discussion.
- <sup>62</sup> Another important issue is agenda setting. In the U.K. and Germany, an external, political entity is responsible for the initial decision regarding which technologies to review and which conditions to prioritize (Clement, et al., 2009; Drummond and Sorenson, 2009; Schlander, 2009; Sorenson, 2010). In Australia and Canada, the agenda is established in response to submissions by manufacturers (Chalkidou et al., 2009; Danzon & Taylor, 2010). Allowing the review agency to set the agenda may help provide information about where research is most needed. A reactive process may help insure that patients receive the most current and effective treatments.
- <sup>63</sup> Hailey (2009); Henry, Hill, and Harris (2005).
- <sup>64</sup> Henry, et al. (2005).
- <sup>65</sup> Fricke & Dauben (2009).
- <sup>66</sup> Gawande's (2009) highly publicized discussion of spending differences between McAllen and El Paso, Texas, has been questioned for failure to consider a number of underlying demographic differences between the communities (Gilden, 2010). Using expense data for patients privately insured by Blue Cross and Blue Shield of Texas, Franzini, Mikhail, and Skinner (2010) report that although Medicare spending per member per year "was 86 percent higher in McAllen than in El Paso, total spending per member per year in McAllen was 7 percent lower than in El Paso for the population insured by Blue Cross and Blue Shield of Texas."
- <sup>67</sup> Doyle (2007); Lorch, et al. (2010).
- <sup>68</sup> Cannon (2009) provides additional critique of the public good rationale for public investment in CER.
- <sup>69</sup> Cogan, Hubbard, and Kessler (2005) provide a relatively recent, policy oriented discussion.
- <sup>70</sup> The 75 percent figure will likely increase in response to reimbursement cuts for Medicare Advantage plans under the PPACA. In principle, Medicare Advantage plans organized as health maintenance organizations or other managed care plans could significantly reduce excessive utilization. In practice, they have tended to provide more generous benefits than the traditional fee-for-service program.
- <sup>71</sup> Consider, for example, a patient and physician dealing with persistent lower back pain with no physical signs of nerve impingement or other symptoms that would indicate surgery. Given substantial fee-for-service insurance coverage (and perhaps malpractice liability concerns), the physician may recommend an MRI exam, even if there is little evidence about the effectiveness of the exam in diagnosing and influencing the course of treatment for the symptoms presented. Physician and prospective patients' willingness to pay for CER on this issue will be low, as will the willingness of insurers given the preferences of patients and physicians.
- <sup>72</sup> Garber and Meltzer (2009).
- <sup>73</sup> Garber and Meltzer (2009).
- <sup>74</sup> Institutions and centers with established infrastructures, expertise, grant-writing capabilities, and intellectual perspectives have a comparative advantage in obtaining funds, if not in priority setting.
- <sup>75</sup> IOM (2009).
- <sup>76</sup> Basu and Philipson (2010).
- <sup>77</sup> Merlis (2010) provides an overview of accountable care organizations and their implementation under the PPACA.
- <sup>78</sup> CBO (2006) provides detailed background on Medicare premium support systems. Also see Cogan, Hubbard, Kessler (2005).
- <sup>79</sup> <http://www.irs.gov/newsroom/article/0,,id=224513,00.html>.
- <sup>80</sup> Peddicord, et al. (2010) discuss this issue and propose a research safe harbor as a solution.

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