

How Will Comparative Effectiveness Research Affect the Quality of Health Care?

Timely Analysis of Immediate Health Policy Issues

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Summary

The health reform legislation recently discussed by Congress would develop an infrastructure for the ongoing generation and dissemination of information on the comparative effectiveness of different health care treatments. The specifics of these proposals have not yet been fully defined, even as the concept of comparative effectiveness raises concerns for many health care stakeholders.

The quality of health care in the United States is uneven, in part because of the lack of reliance on evidence of effectiveness in clinical decision-making. Comparative effectiveness (CE) seeks to produce better information on what health care interventions truly work under what circumstances, and to make this information accessible to physicians, patients and payers.

What is comparative effectiveness?

The Institute of Medicine (IOM) defines CE as the study of methods to “prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care,” including alternative approaches to health care delivery, for the purpose of assisting “consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and the population levels.”

Comparative effectiveness research (CER) refers most often to primary research on the relative merits or outcomes of one intervention, compared to one or more others.

Who is conducting CER?

In the United States, most CER is funded by the Department of Health and Human Services (HHS) and its agencies, the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes for Health (NIH). Historically, less than 0.1 percent of the more than \$2 trillion in annual U.S. health expenditure was allocated to work on comparative effectiveness. The American Recovery and Reinvestment Act of 2009 (ARRA) allocated an additional \$1.1 billion in new CER to be financed by HHS, NIH and AHRQ.

Some CER is privately financed, including proprietary, primary research funded by those with a financial stake in a new health technology, as well as secondary research funded by private insurers seeking to inform their benefits

management programs. Nonprofit organizations and private foundations add to the store of knowledge as well.

Efforts to strengthen the research

Studies have found that much of the CER being undertaken in the United States is not well coordinated, making it difficult to assess the sufficiency and quality of this research. Efforts should be made to:

- Involve patients, clinicians, payers and other decision-makers in CER study development and implementation.
- Improve the research infrastructure to enhance the validity and efficiency of CER studies.
- Develop a range of research methods applicable to CE.

The ARRA authorized the creation of a Federal Coordinating Council for Comparative Effectiveness Research. The health reform bills currently under consideration in Congress would create an entity, either within the government or operating independently, charged with ongoing coordination and prioritization of CER.

Limited current use of CE in benefits decisions

Currently, health coverage programs and payers still define broad categories of covered benefits and cover services that are both “medically necessary” and “not experimental,” using CER to determine whether a particular service meets those thresholds.

The Centers for Medicare and Medicaid Services (CMS) is required by law to cover new medical goods and services that fall within the general categories of benefits and that are considered reasonable and necessary. The Medicare Modernization Act of 2003 restricted the use of comparative effectiveness information in Medicare decision-making and prohibited CMS from restricting coverage to new medicines on the basis of findings from CER. The agency typically does not reject coverage for a technology that is effective, even if it is less effective than an alternative.

How might CE affect health care?

In the best case, enhanced CE will lead to better quality of care and health outcomes by:



- Improving clinical decision-making.
- Assisting patients to get the care they need.

To accomplish this, CE will need to:

- Address topics with important health implications.
- Provide answers to practical questions about the effectiveness of alternative treatments.
- Support the translation of research findings into changes in practice. This will be especially important: in one study the lag between the discovery of more effective forms of treatment and their incorporation into routine patient care was 17 years.

CE may yield cost savings by:

- Demonstrating that some more expensive treatments are not necessarily superior to existing, less expensive treatments.
- Inducing changes in practice that favor cost-effective choices.

Fears about CE relate primarily to the potential misuse of information developed on comparative effectiveness, including concerns that:

- CE will result in rationing of expensive but effective treatment.
- CE will promote government take-over of personal health care decisions. This is unlikely; the government has shown little appetite for intervening in health care decision-making in Medicare, for example.
- CE could promote one-size-fits-all medicine that does not account for the clinical needs of individuals or sub-groups of patients with special needs. If CE is viewed as a tool for informed decision-making, however, individual clinical needs can be considered.
- CE could foster decisions that undervalue the patient's perspective, values, and preferences. Studies can be designed, however, to be more sensitive to such concerns.
- CE will impede the speed of technological development in health care, limiting the prospects for future improvements in treatment as expected profits from investment are curtailed. In fact, CE may lead to decision-making that rewards investment that increases value, and may help build the evidence for the comparative effectiveness of promising technologies.
- CE will hold some drugs and devices to standards of relative effectiveness and cost-effectiveness that are not applied to all services and processes of care. Technologies which have been studied may be rewarded, to the detriment of low-technology changes. These concerns can be addressed by broadly defining the scope of CE.

How will CE be used?

The development of CE information is hardly sufficient to ensure its adoption. Difficulties in accessing and interpreting

research findings and the limited incentives and support for incorporating research findings into practice limit the effect of these findings on clinical decision-making.

While the health reform bills under consideration in Congress would promote and coordinate investment in CER, they actually limit how the information generated can be used.

Serious consideration should therefore be given to:

- Investigating why evidence so often has a limited and slow impact on practice.
- Evaluating policies and practices that improve acceptance of treatments with demonstrated effectiveness.
- Disseminating effective implementation strategies.
- Implementing changes in incentives or other initiatives that prove effective.

The role of costs

Possible options for taking costs into account in conducting and using CE include:

- Using cost as a criterion in selecting topics for CE, and ensuring that CE focuses on areas with the greatest potential to increase the efficiency of health care delivery.
- Including empirical questions about relative cost-effectiveness in research designs.
- Incorporating cost considerations when using CE in medical decision-making.

Neither of the health reform bills that emerged from the House and Senate combine support for CE with authorization of the consideration of costs. Policymakers have been reluctant to discuss what sort of intervention is appropriate, acceptable or desirable to influence a patient's choice of health care treatment. This question much be tackled to define an appropriate role for costs in CE.

Conclusions

There are significant challenges in undertaking a CE initiative, and understandable concerns about CE's having unanticipated and undesirable impacts. Those seeking to further CE should be cognizant of these concerns and make sure that CE activities are transparent to the public. Efforts to distill lessons from extensive past experience in federal work on comparative effectiveness, now extending over at least three decades, should be a priority.

While investing in CE can be a path for improving the quality of health care and increasing the value of health expenditure, we cannot fall into the trap of thinking that just doing the research is enough to change practice, when all evidence suggests that this is far from true. Rather, CE should be considered a valuable part of a larger effort to foster evidence-based medicine, along with changes in incentives and the organization of health-care delivery that are essential to promote and support high-quality health care.

Introduction

Reflecting the view currently popular among analysts that the U.S. health system could benefit from the generation and use of more information on the comparative effectiveness (CE) of alternatives for treating and preventing health conditions, the American Recovery and Reinvestment Act of 2009 (ARRA) took steps towards creating a bigger role for research on CE in the U.S. health system. Congressional health reform proposals would go further to develop an infrastructure for the ongoing prioritization, generation, coordination and dissemination of information on comparative effectiveness. As to how the information is to be used and by whom, with what sorts of institutional supports, very little has been agreed upon, and many of the most promising options for influencing health care practice are subject to strong objections from stakeholders.

Debates about raising the profile of CE have generated a lot of controversy and left open a number of decisions that will determine its impact on health care delivery, quality of care and outcomes. The public debate on these unresolved issues continues, even as public- and private-sector actors move forward to implement those decisions that have been made. The effect gives the impression of a group of travelers starting off on a journey by making a big investment in travel gear, but with disagreement on the intended final destination and the intent to buy a map and to make hotel reservations and transport arrangements along the way. One hopes that it proves to be a rewarding trip, but fears that the failure to plan in advance is likely to result in worthless detours.

This issue brief aims to further the ongoing policy debate by investigating the implications for U.S. health care of an increased role for comparative effectiveness research and related activities. It considers the specific hopes and fears of experts and stakeholders with respect to the prospective impact of CE on quality and outcomes, and

evaluates the basis for those beliefs. It looks at what policy options are on the table, and the implications of various alternatives for quality and outcomes of health care. In so doing, it draws on lessons from U.S. and international experience with CE.

The case for more and better information on what works in health care

The quality of health care depends on providers “doing the right thing, at the right time, for the right person, and having the best possible result.”¹ But research has demonstrated that patients receive only about one-half of the health care that is recommended by medical experts as appropriate for them,² while as much as one-third of certain treatments are unnecessary, inappropriate or even contradicted for the patients who receive them.³ Furthermore, variation in practice across the country is significant, and much larger than can be explained by differences in patient health status alone, indicating that certain procedures are subject to widespread underuse and/or overuse.⁴

Uncertainty as to what is best for patients under particular circumstances is one reason why health care often falls short in terms of quality. Specifically, uncertainty as to the effectiveness (i.e., benefits and risks) of treatments and the relative effectiveness of alternative treatments can and does result in suboptimal care (i.e., underuse, overuse and misuse of health services and medicines) and outcomes.

The persistence of uncertainty can be explained, in part, by important shortfalls in evidence. The Institute of Medicine (IOM) estimates that only half of the treatments and services that comprise standard medical care have been proven to be effective.⁵ And even where a treatment has been proven effective, the degree to which it is more effective than alternative treatments, and the circumstances in which it constitutes a more effective treatment, is often unknown. The U.S. Food and

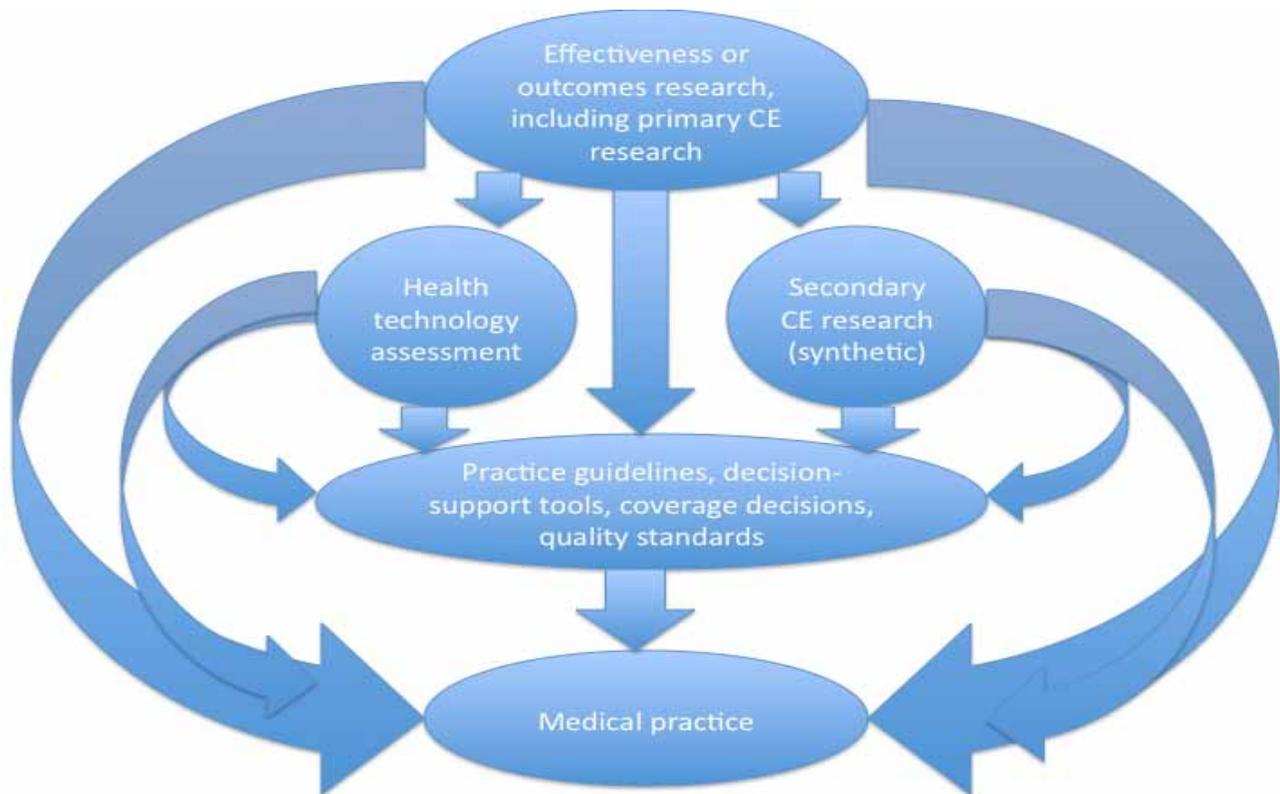
Drug Administration, for example, requires evidence of the efficacy of new medicines, as compared to placebo, but generally does not demand evidence from head-to-head trials with the prevailing treatment.⁶ While some such research is done anyway, there is not enough of it. Furthermore, the information generated through the research is not always used in health-care decisionmaking, both because the comparisons may not be particularly clinically relevant and because such information is not collected and disseminated systematically.⁷ Much of standard practice thus reflects tradition, expert opinion, training, marketing or some combination thereof, rather than application of evidence derived from research related to specific health care options.

In short, the goal of the recent surge of initiatives on comparative effectiveness is to produce more clinically relevant, timely information, relying on new research methods and databases. Such information is more likely to be useful and therefore used routinely by a variety of decisionmakers, including patients, clinicians, and payers. It is important to note that 62 physician organizations signed onto a letter endorsing “a robust, federally sponsored independent Comparative Effectiveness Research (CER) enterprise—one that emphasizes real-life study populations, head-to-head treatment comparisons, and identifying treatments most likely to benefit specific groups of patients—would enable physicians and patients together to make informed decisions.”⁸

What is comparative effectiveness?

Comparative effectiveness is a relatively new term used to designate a type of research and analysis that is not new. As with any new term, different definitions are in use, leading to some lack of clarity in the ongoing policy discussions. In this section we review the key points of similarity and differentiation in definitions, with particular attention to those aspects that have implications for

Figure 1. How Research Affects Medical Practice



Source: Authors.

expectations about the impact of CE on health care delivery.

In 2007, the IOM defined comparative effectiveness as “the comparison of one diagnostic or treatment option to one or more others,”⁹ in this way identifying CE as a subset of a body of work known as outcomes research or effectiveness research, the study of how a health service or technology works in practice, in terms of its impact on patients and patient care. Other definitions put forward by various participants in the ongoing policy debate are similar in describing comparative effectiveness as the study of risks and harms associated with *two or more alternatives* in health care.

Definitions in current use differ primarily in terms of how broadly or narrowly they define the activities that are considered to be part of CE (e.g., observational and/or experimental

research studies, literature review or synthesis), the specification (or not) that CE is confined to clinical considerations or expanded to encompass economic, ethical or other criteria for evaluation, and the possible subjects of CE (e.g., medical services, drugs, devices, therapies, procedures, and even delivery system and work process improvements).

Some definitions (e.g., that of the Medicare Payment Advisory Commission, known as MedPAC) specify that CE is concerned with clinical effectiveness, while others (e.g., that of the American College of Physicians) refer to additional dimensions for comparison, such as safety and cost. Other definitions (e.g., that of the Congressional Budget Office) indicate that CE is intended to compare effectiveness or impact without specifying particular dimensions of study.

The IOM made a further distinction between *primary* comparative effectiveness research, which “involves the direct generation of clinical information on the relative merits or outcomes of one intervention in comparison to one or more others,” and *secondary* CER, which “involves the synthesis of primary studies to allow conclusions to be drawn.”¹⁰ (As illustrated in figure 1, secondary comparative effectiveness research may be considered a type of *health technology assessment*, which examines the medical, economic, social and ethical implications of the incremental value, diffusion and use of an intervention used to promote health.) The distinction is noteworthy in that the term “comparative effectiveness research” is used by some experts and stakeholders to denote primary research exclusively, with synthetic work referred to as CE reviews, analyses or studies.

Historical controversy associated with government CER initiatives

The controversy associated with development of CER is evident from its longer-term history. For example, AHRQ is the reincarnation of an older agency, known from 1989 to 1999 as the Agency for Health Care Policy and Research (AHCPR), which also had a history of work relating to CE, including the development of clinical practice guidelines that drew conclusions based upon synthesis of available evidence on effectiveness and comparative effectiveness. In fact, AHCPR lost its authorization to produce clinical practice guidelines and was very nearly eliminated due to controversy over the legitimacy and value of its clinical practice guidelines.¹ The agency drew fire from back surgeons for its recommendations for treatment of lower-back pain, which were based on findings that the outcomes from surgery were no better than those obtained from medical management of the condition. Another charge leveled by critics, which included public advisory bodies such as the Physician Payment Review Commission and the General Accounting Office, was a lack of evidence that the guidelines had succeeded in influencing medical practice.

AHCPR was not even the first federal government agency to come under fire for controversial work assessing the effectiveness of health care. At least two agencies, the Congressional Office of Technology Assessment and the National Center for Health Care Technology, both succumbed to pressure by opponents of their work. OTA, created in 1972, was dismantled in 1995 after the Republican takeover of the House in the 1994 elections. The National Center was established in 1978 to review evidence on effectiveness and cost of health technologies and to advise on Medicare coverage, as well as to prioritize research, and was dissolved three years later.

¹ Bradford H. Gray, Michael K. Gusmano, and Sara R. Collins, "AHCPR And The Changing Politics of Health Services Research," *Health Affairs* Web Exclusive, June 25, 2003.

In 2009, another IOM committee revisited the earlier IOM definition, broadening it to include the study of methods to "prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care."¹¹ Particularly notable is the extension of the definition to include alternative approaches to health care delivery, which goes beyond what had been encompassed in previous definitions. The 2009 IOM definition further describes the purpose of CER as "to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and the population levels."

Background and recent history of CE in the United States

As discussed above, comparative effectiveness comprises a well-established body of work that predates the current policy interest.¹² Rather than kick-start a new research direction, recent legislative initiatives and current proposals instead address one or more of several objectives: to generate *more* comparative effectiveness research, to see that it is *better prioritized and*

coordinated to meet information needs without duplication, to *apply new research methods* taking advantage of administrative and clinical databases to complement traditional clinical trials to better support clinical decisionmaking, and to *improve dissemination* of research findings to providers and patients with the aim of influencing medical practice. Notably, few legislative initiatives address the intended use of information derived from CER, except to specify ways in which the information is not to be used. A review of the history of U.S. initiatives in this area provides context that helps in understanding the current situation.

Who is conducting CER?

In the United States, CER is funded by the Department of Health and Human Services (HHS) and its agencies. The Agency for Healthcare Research and Quality (AHRQ) largely funds secondary CER, and the National Institutes for Health (NIH) serves as the dominant funder of primary CER, although this type of research has not been a significant contender in terms of NIH priorities. Total funding for health services research in all HHS agencies totaled just \$1.5 billion in 2008, of which a very small share (\$30 million

at AHRQ, plus a small share of funding in other agencies) was devoted to CER. By contrast, the bulk of the NIH annual research budget of \$28 billion is devoted to basic research intended to provide scientific inroads in the prevention and treatment of disease. And in the broadest context, less than 0.1 percent of the more than \$2 trillion in annual U.S. health expenditure was allocated to work on comparative effectiveness.¹³

Complementing the government role in financing research for use by all who can benefit from the information generated, some CER is privately financed, including proprietary, primary research funded by those with a financial stake in a new health technology¹⁴, as well as secondary research funded by private insurers seeking to inform their benefits management programs. Nonprofit organizations and private foundations add to the store of knowledge, as well.

AHRQ's work in CER dates to the Medicare Modernization Act of 2003, which authorized the agency to undertake research to evaluate the clinical effectiveness and appropriateness of health services, so as to improve the quality, effectiveness and efficiency of health care delivered through Medicare, Medicaid and the

State Children's Health Insurance Program. By 2008, the annual budget had doubled to \$30 million.

The provision in ARRA that allocated an additional \$1.1 billion in new CER to be financed by the Department of Health and Human Services (\$400 million) and its agencies, the NIH (\$400 million) and the AHRQ (\$300 million), reflects a consideration that the United States had underinvested in the development of CER.

Not just more research, but better research

Irrespective of whether the volume of CER is socially optimal, another issue is whether CER could be more effective if there were a concerted effort to establish cross-cutting priorities for research, to take stock of and coordinate research efforts, and to highlight the need for research in areas with important information gaps. A recent study by AcademyHealth researchers found that there is a "significant volume" of comparative effectiveness research being undertaken in the United States, but that there is a lack of coordination across and within funding agencies, impeding an assessment of the sufficiency and qualities of the research pool as a whole.¹⁵

Some analysts emphasize the need to fundamentally alter the nature of current comparative effectiveness research to better achieve new expectations by:

- meaningfully involving patients, clinicians, payers and other decisionmakers in key phases of CER study development and implementation;
- improving the research infrastructure to enhance the validity and efficiency of CER studies; and
- developing a range of research methods, grounded in use of empirical data, to replace the traditional "hierarchies of evidence," and its reliance on experimental methods to produce comparative effectiveness evidence.¹⁶

It should be noted that the debate about whether and how to move away from traditional research approaches is not yet resolved, with some parties expressing concern about the limitations of new research approaches, even when acknowledging the problems with the methods generally used, as discussed below.

In ARRA, the Congress created the Federal Coordinating Council for Comparative Effectiveness Research to coordinate comparative effectiveness research and related health services research across the federal government. The council was also charged with advising the President and the Congress on strategies to address the infrastructure needs for CER within the federal government, and organizational expenditures for CER by relevant federal departments and agencies. Furthermore, the legislation directed the council to submit to the President and the Congress a report describing federal activities on CER and recommendations for such research conducted or supported from ARRA funds by June 30, 2009.

Following on this initiative, the health reform bills passed by the House and the Senate would create an entity, charged with ongoing coordination and prioritization of CER.¹⁷ The Senate bill calls for establishment of a semi-independent commission to sponsor CER, whereas the House bill would place CER in AHRQ. Concern has been raised about whether the commissions approach would provide affected industry—device manufacturers and pharmaceutical companies—too great a role in controlling the allocation of funds, the design of studies, and decisions about which results can be published.¹⁸

Is there demand for CE for use in decision-making?

One reason why the coordination role has been unfilled until recently is that, unlike Canada and European countries that have a larger government role in financing and delivery of health services, the United States lacks a

formal infrastructure for making use of CE information to promote evidence-based care. Canada, France, Germany, the Netherlands, Sweden, the United Kingdom and other countries with publicly regulated or administered systems of health coverage have established institutions charged with undertaking secondary CER to inform decisions about coverage of services, including appropriate indications and reimbursement levels for medicines or other services that may be subject to varying co-payment rates, and/or guidelines for prevention and treatment. Although the institutions vary in the scope of responsibilities and in the details of how CE studies are undertaken, such institutions typically identify areas where basic evidence on comparative effectiveness is missing. In some jurisdictions (e.g., Belgium, Ontario, the United Kingdom), such information is used to feed into academic, government and private CE research agendas.^{19, 20}

In the multi-payer environment of the United States, individual programs and payers undertake or commission their own work to synthesize research on effectiveness, comparative effectiveness and costs, to differing degrees. But to a greater extent than exists in many other countries, the ability of both public and private to restrict coverage for a service on the basis of evidence that it is less effective than others, less cost-effective than others, or even ineffective, is relatively limited. Most payers still define broad categories of covered benefits and specify that those services that are both "medically necessary" and "not experimental" are covered.²¹ Primary and secondary CER is used by private payers primarily in determining whether a particular service meets those thresholds, how it should be reimbursed (i.e. awarded a higher reimbursement rate), and whether it can be considered medically necessary in a particular patient's case.^{22, 23}

The Centers for Medicare and Medicaid Services (CMS) is required by law to cover new medical goods

and services that fall within the 55 general categories of benefits and that are considered “reasonable and necessary” for diagnosis or treatment of an illness or injury. Republican and Democratic Administrations have tried unsuccessfully, because of political opposition, to promulgate a Medicare rule to implement this broad congressional directive by specifying specific implementation criteria that could include considerations of comparative effectiveness and even cost-effectiveness for new technology or additional uses for already approved technology.²⁴ Accordingly, at present there are no formal criteria for national coverage decisionmaking in Medicare²⁵ and the agency typically does not reject coverage for a technology that is effective, even if it is less effective than an alternative.

CMS attempts to base coverage decisions of new technologies partly on commissioned health technology assessments to aid in making national coverage decisions. Indeed, a central purpose of the Medicare Evidence Development Coverage Advisory Committee, which advises CMS on coverage decisions, is to define how new technologies proposed for coverage compare to existing ones.²⁶ Despite these intentions, however, a recent analysis of 100 consecutive national coverage decisions found that, in the majority of cases, coverage was approved even though the evidence of effectiveness was considered by reviewers to be only fair or poor. Moreover, the Medicare Modernization Act of 2003 restricted the use of comparative effectiveness information in Medicare decisionmaking by, for example, prohibiting the agency from setting payment rates with respect to relative effectiveness in comparison with existing treatments and prohibited CMS from restricting coverage to new medicines on the basis of findings from CER.²⁷

How might CE affect health care?

An informal survey of writings by experts and stakeholders on their aspirations, concerns and expectations with respect to the prospect of an enhanced role for CE in U.S. health care revealed some common threads. Below we summarize and comment on the hopes and fears associated with CE development.

The hopes...

The most frequently articulated hope or aspiration for enhanced CE is that it will lead to *better quality of care and health outcomes* by improving clinical decisionmaking, achieving more congruence between the care patients need and the care they get. For example, some have argued that CER offers a way to promote identification of the best approaches to medicine that can be adapted to the needs of individual patients (so-called “personalized medicine”) by analyzing the impact of different treatments in subgroups within broader populations.²⁸ To the extent health care can be better targeted to patients’ particular circumstances, it should be possible to obtain better treatment outcomes.

Meeting this expectation for better quality and more personalized medical care requires, first, that CER address topics with important health implications, second, that studies answer practical questions that patients, practitioners, and payers have regarding the effectiveness of alternatives, and third, that research findings are employed in ways leading to changes in practice. While the first two prerequisites seem fully achievable²⁹, based on past experience, the track record with respect to the latter point leaves the prospects for quality improvement uncertain. In fact, medical practice is notoriously slow to change in response to new research findings: one analysis found the lag between the discovery of more effective forms of treatment and their incorporation into routine patient care

averages 17 years.³⁰ Contributing to this lag is the relative lack of effectiveness research under average conditions in diverse populations and clinical practice settings, in contrast to the traditional clinical trials, which typically investigate intervention efficacy under conditions established by research protocols that are not necessarily replicated in practice.³¹

Two examples demonstrate how difficult and slow is change in medical practice in the face of evidence that change can result in dramatic improvements in quality. A fairly recent example is the experience with carotid endarterectomy. Research in the late 1980s found that as many as one-third of patients undergoing this treatment were poor candidates, in that the risks of the surgery exceeded the potential benefits.³² A follow-up study more than a decade later found significant improvement, yet still more than 10 percent of those who underwent the treatment were inappropriate candidates.^{33, 34} Another example relates to the importance of caregivers’ washing their hands prior to patient contact, which was found to reduce infection and deaths as early as the 1840s. Despite prominent research and broad media coverage citing tens of thousands of deaths annually attributed to hospital-acquired infections, compliance with hand washing standards in hospitals ranges from 30 to 50 percent.³⁵

This is not to say that it is impossible to use evidence to change medical care. When research on the use of hormone replacement therapy was interrupted in progress because of findings of increased cardiovascular and cancer risks associated with the treatment, physicians reduced their prescriptions of hormone replacement therapy by 40 percent over a two-year period, for example.³⁶ But in the absence of dramatic and widely reported findings—in this case, easily understandable by the affected patient population—it takes more than mere dissemination of evidence to achieve rapid change. Development of focused interventions geared towards changing practice,

relying on support and incentives, have shown promise, although they are still atypical.³⁷

The second most frequently articulated hope is that CE will yield *cost savings* by demonstrating that certain more expensive treatments (often new versions of available treatments) are not necessarily superior to available, less expensive treatments, and by inducing changes in practice that favor cost-effective choices. Indeed, there is every reason to think that CER will continue to reveal instances in which newer or more invasive treatments—nearly always more expensive—are no more effective than available, less invasive ones, as it has in the past. For example, a 2002 study found that newer drugs known as ACE inhibitors and calcium channel blockers were no more effective than older diuretic medicines in controlling hypertension, despite costing thirty times as much.³⁸ Similarly, a 2006 study found that second-generation anti-psychotic medications, priced at ten times the cost of older products, were no more effective than their predecessors.³⁹

But cost savings will depend on the extent to which not only research findings but also treatment choices favor less expensive alternatives. And here there is reason to question the potential for CE findings, in and of themselves, to result in changes in practice. Indeed, practice is very slow to adapt to new research findings, even in cases where significant cost savings are possible. For instance, the 2002 study of hypertensives has had little impact on practice patterns, reflecting a combination of factors including successful marketing by the manufacturers of their on-patent medicines.⁴⁰ An information campaign sponsored by the National Institutes of Health was largely unsuccessful. Even the cost-conscious Veterans Administration did not require doctors to prescribe diuretics as a first-line treatment because administrators expected too many physicians would request exceptions.⁴¹ While some speculate that increasing pressure to

control costs in the health sector will spur greater use of CER, such pressure has so far failed to produce incentives for patients and physicians to take account of the relative cost of treatment options in clinical decisionmaking .

... and the fears

The list of fears associated with CE activities is a longer one. Many of the fears stem from the concern that increased information about what works will lead to reduced choice at the level of individual patient or doctor, particularly if information about relative cost is used in policy or administrative decisions. Other fears relate to the expectations regarding the conduct and outcomes of CER itself.

A common concern is that CE will result in *rationing* of expensive but effective treatment (either for the population as a whole or for particular populations, such as elderly and disabled Medicare beneficiaries). At present, rationing in the U.S. health system is implicit—individuals with different insurance benefits or with no health insurance face very different costs associated with choice of different options, and some options are unaffordable for some individuals. With few exceptions, the cost of a treatment is not considered legitimate grounds for noncoverage of an effective treatment, although cost-sharing differentiation is used for covered benefits with readily observable differences in cost-effectiveness (e.g., generic versus on-patent medicines). Thus rationing occurs on the basis of willingness and ability to pay. This form of rationing is common to the less-developed countries of the world, where coverage is not universal. But in many developed countries, rationing is more explicit: formal decisionmaking processes are used to define what services and medicines are covered and under what circumstances. In these countries, receipt of market authorization is not sufficient to penetrate the pharmaceutical market, for example; a separate process, which may take into account relative effectiveness and, less commonly, cost-effectiveness,

determines whether the new product or service should be included as a covered benefit and the share of the cost to be paid by the user, if any.

An important difference between the U.S. health system and those of other developed countries lies in the notion of solidarity, however, making it very unlikely that the United States would adopt a system of explicit rationing, irrespective of investment in CE. In tax-financed systems like that used in England's National Health Service, which allocate a fixed budget for services, the population generally accepts⁴² that choices must be made; financing a costly treatment that extends the life of a terminally ill patient for weeks or months must be weighed against the value of financing more hip replacements that improve the quality of life for recipients. In a largely privately financed system like that of the United States, by contrast, coverage expansion results in cost and premium increases that increasingly render insurance unaffordable for some, but there is relatively little social pressure to make decisions that increase the value or efficiency of collective health expenditures.

In this respect, the United States is not dissimilar from those health systems of western Europe that are financed by social insurance, which tend to have comprehensive coverage schemes and tend to squeeze prices and fees, rather than limit access to services. When using CER in coverage, pricing or reimbursement decisions, questions of cost impact and cost-effectiveness are not always subject to explicit, formal consideration. In some countries, including France and, up until recently, Germany, decisionmakers are not authorized to consider cost-effectiveness in coverage decisions (and in the technology assessments prepared to support the decisions).⁴³

If explicit rationing in the U.S. health system is unlikely, the threat of a closely related concern is that CE will promote *government take-over* of personal health care decisions is also minimal.

In administering the publicly financed Medicare program, the government has shown little appetite for intervening in health-care decisionmaking and hesitates to use information on relative effectiveness to restrict coverage. Absent the Congress providing explicit authority to do so, there is no basis for thinking that investing in more information will change that position, although pressure for more intervention in Medicare could increase as cost growth threatens program sustainability. In terms of influence on private coverage, the government has neither the incentive nor the means to interfere in health-care decisions. Even in countries, like the United Kingdom, which make formal use of CE in determining whether a product or service constitutes a covered benefit that is financed collectively, there tends to be no interference with clinical autonomy in determining what care is appropriate for a patient in a given case.⁴⁴ This stands in contrast to the practice of insurers in the United States, many of whom employ management practices such as prior authorization and post-utilization review, which challenge the judgment of health care practitioners, for better or worse, and sometimes result in denial of payment.

Another concern is that CE could promote *one-size-fits-all medicine* that does not account for the clinical needs of individuals and/or sub-groups of patients with special needs, i.e., personalized medicine. Here the concern is that CER studies themselves cannot readily include patients with complex cases and multiple conditions, some of whom might have different experience with particular treatments. The validity of this concern depends on the extent to which CE is used to limit treatment options, as opposed to helping to promote informed decisionmaking under particular circumstances.

Additional concerns relate to the potential for CE to foster decisions that undervalue *the patient perspective, values, and preferences*. Here, much depends on the way in which CE

studies are designed. Some focus primarily on clinical outcomes such as reductions in mortality and morbidity. They may not be designed to take into account aspects of a treatment that patients value, regardless of whether they have an apparent and significant health impact. Examples include preferences for oral administration of a medicine or reduced frequency of administration, which might influence patient compliance and, thus, outcomes. But studies can be designed to be more sensitive to such concerns; inclusion of patient representation in establishing frameworks for study design may help.

Another argument against CE is that it will *impede the speed of technological development* in health care, limiting the prospects for future improvements in treatment, to the extent that expected profits from investment are curtailed. However, even with the massive increase in CE spending under ARRA, total expenditures on CER account for just 1.5 percent of the \$100 billion invested annually in R&D and regulatory approval for new technologies.⁴⁵ While it is true that reduced expectations for returns on investment would be expected to reduce the overall level of investment, it is also true that decisionmaking that better rewards valued investment (e.g., those innovations that offer important benefits) would provide investors with incentives to focus R&D on areas where there is the most potential to develop innovation that is most wanted and needed.⁴⁶ And coverage decisions can provide support for emerging technologies by financing treatment in head-to-head trials for promising technologies where evidence on comparative effectiveness is lacking and needed.

A final concern is that CE will contribute to *allocative inefficiency* in health expenditure by holding specific technologies (drugs and devices) to standards of relative effectiveness and possibly cost effectiveness that are not applied to all services and processes of care. On the other hand, some have

argued that a strict regime of evidence-based coverage would tend to reward technologies which have been studied—primarily drugs, devices or other technologies where there is a potential for the study's funder to reap monopoly profits from adoption and diffusion—and create a bias against low-technology changes, such as new uses for a generic drug, a better diagnostic strategy, or improvements in delivering care.⁴⁷ These concerns provide a good argument to define the scope of CE broadly, using agreed criteria for prioritizing among the plethora of possible topics. Of the 100 priorities recommended for study by the IOM Committee responding to the ARRA mandate to develop initial national priorities for CER, almost half were topics involving delivery of care or work process alternatives.

In sum, the fears associated with CE are very much related to the potential misuse of information developed on comparative effectiveness. They can be averted by recognizing that CE provides useful information and valuable input for making decisions that would otherwise be made in the absence of information, but that good decisions depend on sound decisionmaking as well as on good input.

Determinants of the impact of CE: Policy issues and options

The extent to which CE meets the hopes and avoids the risks discussed above depends largely on decisions made in several key areas. We review these policy issues and options below.

How will CE be used?

Some discussions of CER seem to take for granted the assumption that well-designed research with important findings will be sure to influence health care. But the fact is that development of CER information is hardly sufficient to ensure its uptake. Difficulties in accessing and interpreting research findings and the limited incentives and support for incorporating findings into practice contribute to the slow

rate at which research findings are incorporated in medical practice. It is presumably for this reason that the Congressional Budget Office (CBO) did not assume major savings from a major investment in CER on health care costs.⁴⁸ CBO speculated that the impact of CER might be larger if there were incentives and processes for more rapid and effective transfer of CER findings into the practice of medicine.⁴⁹

Current research is often not designed or presented in ways intended to address the practical questions of relative benefits and risks that most concern patients, physicians and other decisionmakers. Furthermore, practicing physicians and others whose decisions or behavior could be influenced by information on CE do not always have time to keep current with the plethora of studies published in the peer-reviewed journals and other outlets, even within a particular specialty.

CE research has increased impact when it has been synthesized and interpreted for intended users of the information, including health care professionals, patients, and administrators.⁵⁰ Many authorities and interested parties do work to bring information from comparative effectiveness research to intended audiences by producing clinical practice guidelines, patient information tools and health technology assessment reports for use by hospital administrators, insurers and others responsible for purchasing or benefits decisions. Still, the incentives to use information on CE in decisionmaking are weaker than they might be. For the most part, coverage, reimbursement and provider payment schemes have not been designed to promote and ensure high-quality care, but to meet other objectives (e.g., cost control, profit maximization).

In her influential *Health Affairs* article of 2006, health economist Gail Wilensky made an argument on the need for creating a new comparative effectiveness center charged with producing primary CER, but noted that “better information about the

comparative effectiveness of various medical strategies and procedures might not, in itself, lead to better decision making in health care unless there is also a major change in financial incentives.”

Indeed, at present, few actors in the health care system face strong incentives to seek out and use evidence from CER. Private health insurers, for example, can pass on the costs of new technologies in premium increases and face little competitive pressure to limit the package of covered benefits. Practitioners are largely remunerated on a fee-for-service basis and are not held accountable for health outcomes or even adherence to up-to-date standards of care. In fact, research on the impact of eight of Medicare’s local coverage decisions found no statistically significant changes in practice relating to seven of the decisions following the implementation of a new coverage policy.^{51, 52} Patients have perhaps the greatest incentives, but relatively few are equipped to make use of the highly technical scientific evidence generated through CER and to understand how it applies to their particular situation.

The specific channels through which the enhanced investment in CE that has been made through ARRA are expected to effect changes in medical practice are undefined and unclear at present. While many of the health reform bills under consideration in the House and Senate would take further steps to promote and coordinate investment in CER, the bills would actually limit how the information generated can be used.

So far there have been more indications about how CE is not to be used than the contrary. For example, the conference report from ARRA notes that the “conferees do not intend for the CER finding to be used to mandate coverage, reimbursement, or other policies for any public or private payer.”⁵³ Similarly, both the House and Senate health reform bills contain language that would prohibit the use of CER findings to deny or ration care, or to make coverage decisions in Medicare.

Some stakeholders do see a role for CER information in policy decisionmaking, however. As part of its recommendations calling for the creation of a new entity to manage CER, MedPAC stated that the new entity would have “no role” in “making or recommending coverage decisions for payers”⁵⁴ but does point to ways in which CMS might use the information generated through CER in both coverage decisions and payment design (e.g., through development of a tiered cost-sharing structure).

A strong argument could be made that, however great the potential importance of new research findings to be generated through new CER, there is greater marginal value to be gained from devoting additional resources to investigating why evidence so often has a limited and slow impact on practice, evaluating policies and practices that improve uptake of treatments with demonstrated effectiveness, disseminating effective implementation strategies, and implementing changes in incentives or other initiatives that prove effective. An illustration of this potential relates to the prescription of anticoagulant therapy for patients with atrial fibrillation. Despite publication of several research studies since 1989 indicating that this therapy reduces risk of ischemic stroke by 68 percent or more, anticoagulants are still not prescribed for most patients in whom such treatment is indicated.⁵⁵ Very recently, a new study has been published showing that a new, on-patent anti-coagulant offers modest but statistically significant improvement in effectiveness over a medication for which the patent has expired. While some patients should benefit from the new research findings, to the extent that physicians prescribe the new treatment in place of the old, many more could benefit if either therapy was prescribed to a higher share of suitable candidates.

How and when, if at all, should cost considerations come into play?

One of the most contentious questions that arises in discussion of comparative effectiveness policy issues is that

of when, how, and even whether costs should be taken into account in undertaking CE and in using it in decisionmaking. There are a number of options, not mutually exclusive, for introducing cost considerations, ranging from using cost as a criterion in selecting topics for CE, to early inclusion of empirical questions about relative cost-effectiveness in research to incorporating cost considerations when using CE in decisionmaking. On the other hand, it is also entirely possible to proceed with a CE program that features no formal or even informal role for cost considerations.

Including cost as a criterion for the selection of topics on which to undertake CER offers potential for helping to focus on areas with great potential to increase the efficiency of health-care delivery, although that does not, in and of itself, serve to aid in identifying cost-effective treatment options. There is precedent for including cost impact as a criterion for selecting topics for investment in CER. The IOM committee responsible for developing a list of priority projects for research included the cost of a particular condition as a criterion for the committee's consideration in selecting the most meritorious topics for research.⁵⁶ Similarly, in its June 2009 report, the Federal Coordinating Council on CER recommended that prospective CER studies be prioritized in terms of their potential impact in a number of areas, including cost.

Going beyond topic selection, there is an argument for including cost studies as part of original research on effectiveness and comparative effectiveness, and an even stronger argument for including it in synthetic studies, using formal cost-effectiveness analysis or merely collecting and reporting data on the costs associated with alternatives.

Absent such efforts, there are increased odds of not having the information for decisionmaking when needed. Further, information on a new product's relative cost-effectiveness has potential to promote value even without the extreme option of restricting coverage in cases

where there is no evidence of enhanced benefit or advantage to patients from a higher-cost alternative. It could be used to steer service choices to higher value by designating lower-cost, first-line treatments, for example.

That said, the policy debate has veered in the direction of noninclusion. For example, the legislation that authorizes the AHRQ to conduct CER does not provide the agency with the authority to evaluate the cost-effectiveness of treatments. Of the health reform bills considered in the Congress, none that call for development of a new center for promulgating CER also authorizes consideration of costs, although such consideration was envisaged in a legislative proposal created by former Majority Leaders Baker, Daschle and Dole.⁵⁷

Information on a new product's relative cost-effectiveness has potential to promote value even without the extreme option of restricting coverage in cases where there is no evidence of enhanced benefit or advantage to patients from a higher-cost alternative. It could be used to steer service choices to higher value by designating lower-cost first-line treatments, for example. The U.S. Congressional Budget Office concluded that CMS would need new authority to explicitly consider relative benefits and costs if CER is to have a sizeable impact on Medicare spending, however.⁵⁸ Such authority could have advantages beyond the direct impact on Medicare spending, in that Medicare's initiative could drive other payers to take further steps along this road, following a perception that government actions have increased the legitimacy of cost considerations in coverage. However, judging from the recent trend, as discussed above, it seems that the Congress is more inclined to forbid that Medicare consider costs in coverage decision making.

The question of costs and whether something is worth the cost also arise, obviously, in other areas of policy-making in the United States. In the environmental area, for example, formal cost-benefit analyses are sometimes used to evaluate prospective regulations prior

to their promulgation. But these rules apply generally to the whole population, not to specific patients, who would have to bear the cost of decisions not to cover treatments that are marginally effective, if not cost-effective; explicit consideration of costs relative to benefits seems particularly controversial in the health area.⁵⁹

Part of the problem may be a failure to engage sufficiently in debate over the question of what sort of intervention is appropriate, acceptable or desirable to influence a patient's choice of health care treatment in the case of alternatives that differ in terms of prospective impact on both health and cost. The default position is that a patient should have whatever his health care practitioner considers clinically appropriate and that he can afford to pay for. In the face of widespread health insurance that pools resources to meet the costs of care for insured individuals, the question arises as to whether added costs for treatments that are not proven more effective than alternatives should be borne collectively, or by the individual who chooses the alternative. And in the face of publicly financed coverage for which the government is accountable to the taxpayer for efficient allocation of finite resources, the question arises as to whether the government has a responsibility to direct the use of public funds to care that provides greatest benefit, relative to its cost. Without such a dialogue, it may prove impossible to establish explicit cost considerations within the context of the current U.S. health system.

Conclusions

Several conclusions can be drawn from the review undertaken in this brief.

U.S. history and international experience show that there will be significant challenges that must be carefully addressed if the latest CE initiative is to succeed. There are understandable fears and concerns about CER having unanticipated and undesirable impacts. The evolution of activities to further CER should be cognizant of these concerns and remain transparent to

the public. Efforts to distill lessons from extensive past experience in federal work on comparative effectiveness, now extending over at least three decades, should be a priority to avoid knowable pitfalls.

There is a need to proceed with clear objectives and a plan for accomplishing them. Unless we develop a plan for using CE that goes beyond mere dissemination to ensure practical implementation of findings, there is a risk that resources that have been invested will not have the impact on medical practice that

they could and should have. While elaborating such a plan is beyond the scope of the present brief, there is much to draw upon from successful quality improvement experience, including experience showing that changed incentives, together with organizational support for practicing evidence-based medicine, can yield impressive results in institutions (hospitals, group practices) that have launched successful initiatives. It behooves policy makers to ensure that the health care financing and delivery environment is generally conducive to such initiatives.

While investing in CE can be a path for improving the quality of health care and increasing the value of health expenditure, we cannot fall into the trap of thinking that just doing the research is enough to change practice, when all evidence suggests that this is far from true. Rather, CE should be considered a potentially important part of a bigger effort to foster evidence-based medicine, along with changes in incentives and the organization of health-care delivery that are needed to promote and support high-quality health care.

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