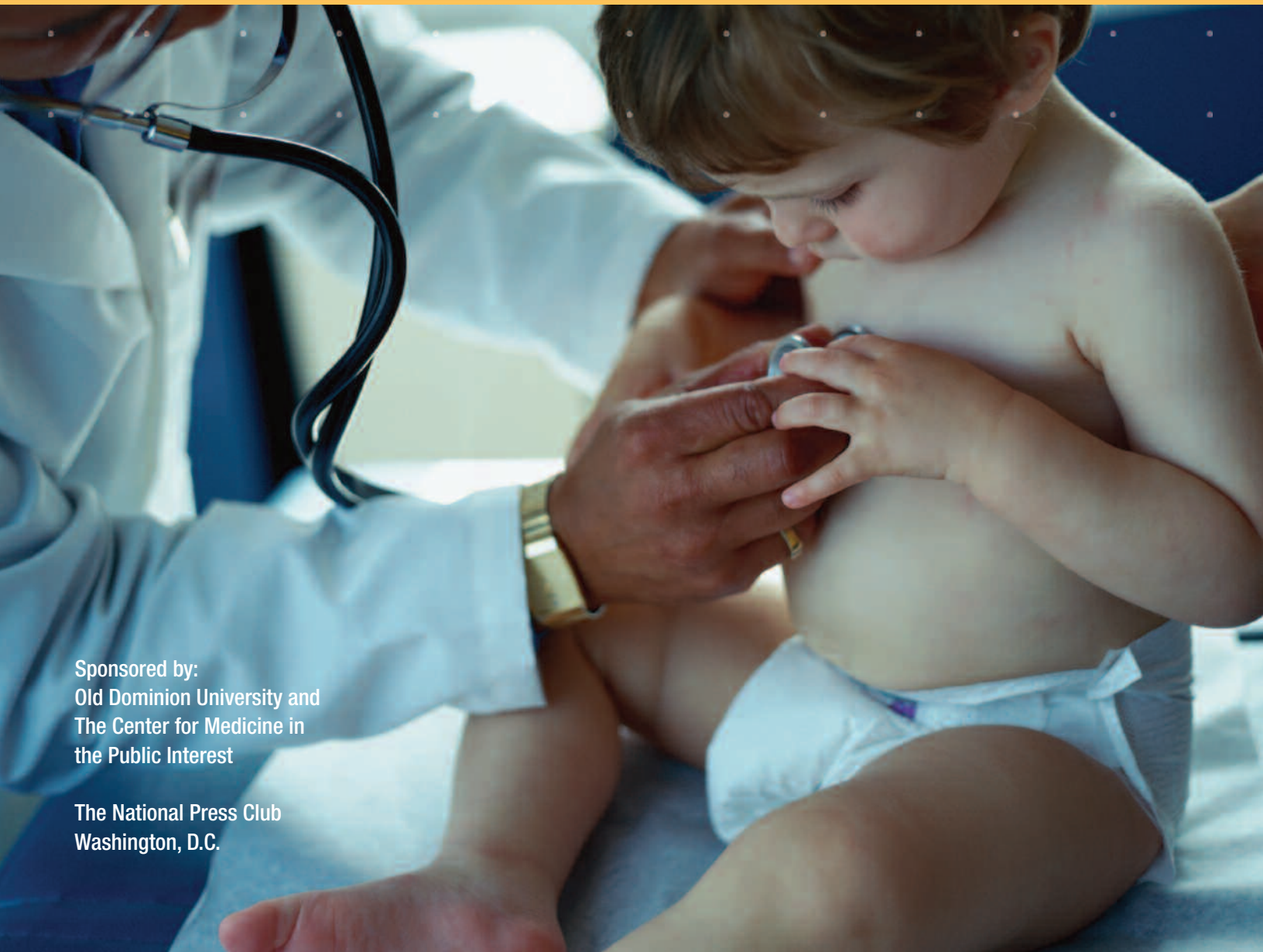


Improving Health Care Quality and Value: The Role of Comparative Effectiveness Research 2007

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Improving Health Care Quality and Value: The Role of Comparative Effectiveness Research

Comparative Effectiveness Research (CER) is in the spotlight as a tool for addressing health care quality and improving health care value. By closing gaps in evidence, this type of research can enable health care decision making by patients, providers and policy makers. However, many basic elements of the issue are neither clearly defined nor well understood. Given the growing interest in policies to expand the government’s role in CER, it is very important for all stakeholders to identify and address key unresolved issues. To advance understanding of CER, Old Dominion University and the Center for Medicine in the Public Interest sponsored a forum in 2007 in Washington, DC: “Improving Health Care Quality and Value: The Role of Comparative Effectiveness Research.” Attending were panelists from the government and private sector who are experts in the fields of health care policy and economics policy, medical research, and patient care.

During the Forum, several major themes emerged. Specifically, participants highlighted the importance of:

- clearly defining the goals of CER;
- establishing open, effective, patient-centered processes for research priority-setting and application of results;
- defining the scope of CER; and
- addressing significant gaps in research methods.

The report that follows summarizes panelist comments on each issue and theme.

Comparative Effectiveness Research: Conference Conclusions	
Key Issues	Major Themes
CER Goals	<ul style="list-style-type: none"> • Be patient-centered • Inform clinical practice • Clearly communicate results to all stakeholders • Support quality and value, not simply cost containment • Support scientific advances, health information technology, and the emerging science of personalized medicine • Receive collaborative stakeholder support in a transparent manner
CER Scope	<ul style="list-style-type: none"> • Include clinical practice and therapies • Support Health Information Technology (HIT), personalized medicine
CER Methods	<ul style="list-style-type: none"> • Move beyond prospective, randomized clinical trials (RCTs) • Consider prospective “practical” clinical trials and observational data • Address validity and applicability of findings

Important Questions

Dr. E. Andrew Balas of Old Dominion University College of Health Services identified five key questions for today's CER:

1. What are the right questions and the appropriate triggers for research?
2. What are the right kinds of research: RCTs, meta-analyses of RCTs, observational trials, "practical" clinical trials?
3. Are available research methods/mechanisms adequate to provide credible, peer-reviewed results?
4. How should findings be applied at the individual and policy levels?
5. Is public health well served by major differences in levels of scrutiny for different types of clinical interventions?

Historical Context

The concept of a governmental or quasi-governmental role in assessing and comparing outcomes of different health care interventions is not new. Since the 1960s many government and private sector entities have had this focus. According to Dr. Bryan Luce of United BioSource Corporation, such efforts have had four very different goals:

- improving health;
- improving information for health decision-making;
- improving value; and
- overt or implicit cost control.

For example, the Oregon Drug Effectiveness Review Project (DERP), whose reports currently guide decisions in 13 Medicaid agencies, has stated goals of improving health and decision-making. However, Medicaid agencies have used the information to establish Preferred Drug Lists that control costs.

Goals of Comparative Effectiveness Research

Forum panelists emphasized that goals of CER must be clearly defined to inform sound policy on government support for CER. Major goals identified by panelists included:

- ensuring a focus on patient/clinical needs, and
- appropriately balancing these needs with economic considerations in the broader health care context.

Speakers also noted that policy on CER should support emerging medical innovations, including health information technology and the science of personalized medicine.

Achieving Patient-Centered CER

Speakers identified several key areas of focus in developing patient-centered CER programs. These included the scope of research; setting research priorities; communicating results, and applying results.

According to Dr. Carolyn Clancy, Director of HHS' Agency for Health care Research and Quality (AHRQ), the only way to improve value in health care is to focus on meeting patients' needs. AHRQ approaches CER with a goal of supporting patients and clinicians in selecting the best treatments to meet patients' needs and preferences. As a result, AHRQ works to set research priorities based on diseases and conditions,

"I think we are at the end of the beginning [of the debate about comparative effectiveness research] where at least we can all agree that this is not and must not be exclusively a debate about saving money. It must be about patient care."

PETER PITTS

rather than specific interventions. Dr. Clancy said she believed CER could be performed in ways that were both patient- and cost-centric, and that the critical issue is determining how to make sure that science informs patients and clinicians so individuals receive the treatments that best meet their needs and preferences.

Jennifer Bright, of the National Working Group on Evidence-Based Health care, noted that a major goal of CER efforts should be to enable patients to play a central role in conversations and decisions about their own health care, health care research, and health care policy. Patient roles can include helping to:

- develop relevant research questions;
- discuss the values that should drive health care decisions;
- evaluate therapies or procedures by participating on relevant committees; and
- disseminate research results through advocacy groups.

She said, “Starting and ending with the patient is absolutely the right way.”

“Our organization truly believes that in order to get a patient-centered system, you need to put that patient in the driver’s seat from the get-go.”

JENNIFER BRIGHT

Dr. John Bridges, of Johns Hopkins University, said that evidence-based medicine, outcomes research, health technology assessment (HTA) and related efforts have “changed the quality of medicine for the better.” However, he believed they are flawed because they take a top-down, societal perspective to health care decision-making. Noting that “patient-centeredness” is one of the six aims of health care identified by the Institute of Medicine, Dr. Bridges called for a reevaluation of evidence-based medicine (EBM) and HTA to make them patient-based. Dr. Bridges said this would require departing from current doctrines (collective provision, collective financing and paternalism), assumptions (the societal

“The only way we get to what I’m going to call smart health care—that is, better value in health care—is if we are focused on what meets patients’ needs.”

CAROLYN CLANCY

perspective, scarce resources and opportunity costs, and asymmetrical information), and methods (randomized controlled trials, cost-effectiveness analysis and “quality-adjusted life-years”). He defined patient-based EBM/HTA as:

- focusing on the patient’s problems;
- taking a patient’s perspective;
- accommodating of the patient’s preferences;
- allowing patient participation;
- building upon patient/physician partnerships; and
- empowering the patient to improve their health.

Support Better Quality and Value, De-emphasize Cost-Containment

Citing projections that health care spending will consume a growing percentage of the U.S. gross domestic product and the federal budget, Dr. Wilensky of Project HOPE, said that CER results can improve value for consumers and payers by enabling better clinical and health care spending decisions. Dr. Wilensky called for creation of a new entity to support research on comparative clinical effectiveness, saying this is one of the fundamental steps needed to “learn how to spend smarter” in health care. However, she emphasized, the new entity should not be a decision-making center, and should not conduct cost-effectiveness research. She said information analyzed and disseminated by the center would have to be objective, timely, transparent, and clear to the relevant audience.

Panelists also cautioned against over-reliance on CER alone as a solution for addressing quality and cost challenges in health care. Expanding CER “is not the only thing that needs to be done to learn how to spend smarter,” Dr. Wilensky said. “We need to fundamentally realign financial incentives” and “involve consumers much more in the decision making” as well.

“The objective of the effort is also important and it needs to be on the table. [While cost is a factor,] it’s commonly not said that way. A good example is the Drug Effectiveness Review Project in Oregon is specifically not about cost, but the evidence is used specifically for cost control and preferred drug lists and ‘best buys’ and so forth.”

BRYAN LUCE

Dr. Drozda, with the Centene Corporation, concluded that CER data should be used as one element of health care coverage management, but used with caution. He recalled that when U.S. managed care organizations in the 1990s created tiered coverage schemes for tests and therapies (“you must try X before you will be covered for Y”), limiting access to minimize costs proved politically unpopular. The cultural value Americans place on access is a strong barrier to cost-centric uses of CER.

Similarly, he stated that CER information alone should not guide physician incentive schemes. Experience shows that offering monetary rewards for hitting a specific target will increase the number of physicians that reach the goal. However, given patient variation, current CER results based on RCTs do not apply to all individuals. Hitting a target based on such data may not improve outcomes. Dr. Drozda cautioned against the danger of “getting a little lost in the area of CER as maybe being an end in and of itself, when actually it is only one tool to be used in the reform of health care.”

CER Should Support Scientific Innovation, Health Information Technology (HIT), and Advances in Personalized Medicine

Using new technology for CER, the Mayo Clinic’s Dr. Peter Elkin believes we can move from the slow, periodic dissemination of research data into practice to rapid, regular information-sharing for continuous improvement; and from clinical practices based on RCT group outcomes to personalized medicine. Furthermore, he stated, the rapid dispersal of innovations for personalized care has the potential to improve treatments, and health, and reduce clinical trial failure rates by enabling more targeted participant selection.

To support personalized care and improved health outcomes, Dr. Elkin made the point that HIT initiatives should be concerned with all facets of health research. This includes clinical research, basic science, population research, environmental sciences, bioengineering, and informatics. AstraZeneca Pharmaceuticals’ Dr. Wayne Rosenkrans, Jr. said that HIT is the key to creating an infrastructure for a “learning health care system.” This system would constantly generate shared data on CER leading to appropriate, personalized medical decisions. For the pharmaceutical industry, continuous data-generation and education could dissolve the barriers between the current artificial “silos” of phased research, allowing data to continuously recirculate into medical practice creating earlier benefits for patients and better value for industry. He noted that computerized decision-support systems paired with electronic medical records have been shown to improve adherence to clinical guidelines among patients and providers. These records can help patients own and understand their health information and status, enhancing participation in their own care.

“We have the developments of technology happening along one axis, the developments in research practice along another; we need to get them to merge.”

PETER ELKIN

The Scope of CER

One of the important themes discussed at the Forum was the scope of government-supported CER efforts. Participants described a broad research agenda covering a variety of

medical technologies and health care interventions. In some cases this included research on different health plan and benefit design options, as well as approaches to the management, organization and delivery of care. Participants also discussed different types of research that might be included under government programs for CER (for example, whether to include cost-effectiveness research, and how findings from observational studies fit with results from randomized clinical trials) and how these might change in the future.

The scope of CER should encompass topics throughout the health care system. Dr. Luce described how past CER endeavors often have concentrated on comparing drugs because pharmaceutical companies fund extensive research to meet FDA regulatory requirements. Therefore, a disproportionately large quantity of evidence is available for pharmaceuticals, making it easier to conduct comparative analyses. Dr. Wilensky agreed and noted that such studies have an important limitation for guiding health care decisions: they typically compare an intervention to a placebo, or sometimes to the existing standard of care, but rarely to the relevant clinical alternatives for patients and their physicians. Dr. Wilensky also said that FDA regulation only covers drugs and devices. A far greater percentage of health care costs is allotted to medical procedures, surgery, and other interventions. More CER in these areas is critical, she believes, and may benefit from the creation of a new agency specifically tasked with this priority.

Dr. Drozda added that CER should not focus solely on new medical technologies. For example, studies comparing approaches for using existing medical knowledge to improve hypertension or diabetes control could potentially improve health and reduce health care costs. Peter Pitts agreed that it is important to consider how CER can help improve health care quality. “When you consider the vast amounts of patients... with untreated diabetes, hypertension, and high cholesterol,

“While drugs and devices are important to understand their comparative clinical effectiveness, I’m an economist that very much believes in the Willy Sutton principle, which is you go to where the money is. And that’s not where the money is, fundamentally.”

GAIL WILENSKY

you have to think to yourself, what can we do best to make sure that the right patients get the right treatment at the right time?”

Research Questions

Several forum speakers discussed the importance of defining new, patient-centered models for setting federal research priorities.

“Oftentimes you see models of how to include patients in the continuum of knowledge, and we’re usually at the tail end in the translation and dissemination end. Well, I would argue that we need to be upfront and sitting with researchers and developing the research questions that need to be asked and answered,” advised Jennifer Bright.

Researchers should approach CER from the patient’s point of view, rather than from a top-down societal perspective, according to Dr. Bridges. The driving questions should be:

- what are patients’ unmet problems and needs;
- what do patients prefer (e.g., medical devices or pharmaceuticals, pharmaceuticals or medical procedures); and
- what do patients want and need to know?

Scientific methods are available and should be employed to evaluate and incorporate patient preferences.

“Studies comparing approaches for using existing medical knowledge to improve hypertension or diabetes control could potentially improve health and reduce health care costs.”

JOE DROZDA

Ms. Bright said that CER using patient-oriented outcome measures could help motivate better patient adherence to treatment. In addition, she suggested that patient-centric CER could address the many unanswered questions about how race/ethnicity, age, and gender affect treatment outcomes.

The key to useful CER is asking questions that concern patient care decisions. Dr. Scott Gottlieb, of the American Enterprise Institute, described how many CER studies have produced no significant medical practice change, because they have not answered clinicians' information needs. For example, results of studies that determine the relative effectiveness of two drugs for a given condition may be irrelevant when the operative question for physicians is whether the two can be safely combined for greater efficacy. To achieve the goals of patient-centric CER and obtain answers to significant clinical questions, sponsors should involve clinicians in question development. If Washington policy makers generate the questions, he said, the goals are more likely to be cost-centric.

According to Dr. Gottlieb, "I think it comes down to the fundamental question of who's generating the questions that you're pursuing. If the questions that are being pursued when it comes to trying to look at comparative effectiveness kinds of issues are questions that are generated here in Washington, it's going to be a cost-centric exercise. It will not be a patient-centric exercise, it will not emanate from the practice of medicine."

Citing examples of recent large comparative trials of high blood pressure drugs and schizophrenia drugs, Gottlieb said "we spent hundreds of millions of dollars on these studies and they really didn't change clinical practice that much. And the reason why they didn't change clinical practice that much isn't because the information that they generated wasn't additive to the kinds of clinical considerations that physicians made; certainly incremental information that comes out of rigorous trials is always beneficial to clinical practice. But fundamentally, the kinds of scenarios that those trials set up weren't the kinds of scenarios that doctors were facing in their clinical practice."

"I would propose that the ideal place for generating those kinds of questions about, what are the most important scenarios that people face [is not a government agency]. I think it's really in clinical practice with the clinicians who are confronting these questions."

SCOTT GOTTLIEB

Research Methods

Panelists identified significant research method issues that must be addressed in order to expand CER. They noted particular challenges in transcending randomized, controlled trials to use of other research methods like observational studies.

Panelists agreed that progress toward personalized medicine and patient-centric care requires moving beyond a sole focus on randomized clinical trials. While these trials are important to understand the effects of interventions, they cannot answer all questions related to use of those interventions in actual patient care. Speakers also agreed that other types of real world studies pose the substantial challenges of ensuring valid results, and may lack credibility with some audiences.

Dr. Luce reviewed other actual and potential research approaches for CER. None of the past, and few current assessment initiatives involve unblinded and uncontrolled prospective clinical trials. While approaches like "practical" clinical trials have the advantage of more closely reflecting real-life medical practice and all populations, "there are clearly issues with how you go about that from a methodological standpoint," he said.

Other potentially useful methods include observational studies (prospective studies of patient registries or retrospective studies of clinical and claims data), and the broad literature reviews and secondary data analyses using clinical data sets that AHRQ's evidence-based practice centers and DECIDE centers use.

“There’s a great difference in terms of the scope of evidence, the design, the effort, and the funding involved. I think it’s critical to specify and to understand what is intended when you hear the term [CER].”

BRYAN LUCE

According to Dr. Gottlieb, criteria for selecting research methods should include the cost of undertaking the research as well as research validity. Large RCTs can cost hundreds of millions of dollars. Less expensive studies can provide useful information if sponsors create rigorous mechanisms for data use. For example, the FDA has developed guidelines on the use of retrospective epidemiologic data in answering drug safety questions. Dr. Gottlieb believes it will also be important to allow new technology developers, who offer a uniquely informed perspective, to participate in the discourse.

“What kind of evidence are we going to try to ultimately generate?” Dr. Gottlieb asked. “Retrospective analysis, epidemiological data sets, registries?” Or “very rigorous, randomized placebo-controlled trials, prospective trials? If we rely on the latter, it’s going to be exceedingly expensive. But if we rely on the epidemiological data, we need to concede the fact that we are relying on a less rigorous data standard that ultimately is less reliable. So it is very important that we discern, I think, upfront what our methodology is going to be, and how to go about that methodology in a rigorous fashion.”

Dr. Luce emphasized that research sponsors must carefully address validity issues when selecting research methods. He noted that a large U.S. constituency believes that only

blinded, randomized RCTs produce valid information. While many health services researchers see observational data as a valid tool, others, including the FDA, would view it as biased. CER can succeed in supporting public policy only when perceived as credible. Efforts like those pursued by the Office of Technology Assessment ended when critics attacked the credibility of their research and goals.

Health Information Technology

Several panelists addressed the possible role of HIT for advancing CER and personalized medicine. Key advantages included its potential to accelerate research, support personalized care, and create a “continuous learning” model for the health care system.

Accelerate Research

Dr. Clancy reported that ARHQ is creating a public-private partnership to enable the use of electronic patient health records for CER. Initial goals are to establish common definitions for data organization and storage. While each partner organization will maintain its own data, they will share data for cooperative research projects. One major advantage will be the ability to locate appropriate patients quickly for accelerated studies of breakthrough treatments, such as cancer therapies targeted to small patient subgroups. Other potential directions may be to develop (or pre-populate) patient registries from clinical information systems and learn more about the results of off-label uses of medications.

Support Personalized Care

To support personalized care and improved health outcomes, Dr. Elkin said that HIT initiatives should be concerned with all facets of health research, including clinical research, basic science, population research, environmental sciences, bio-

“The RCT is an excellent methodology if you want to understand how, on average, one treatment is better than another...[But] no single person in the health care system is the average...so this is not conducive to...personalized medicine...You want to know, ‘What’s happening for me?’”

JOHN BRIDGES

engineering, and informatics. To build a national HIT-based research framework that supports personalized care and improved outcomes, he believes key steps include:

- build data repositories and ontologies for quality monitoring to encourage reuse of data;
- create a national IRB standard, which does not currently exist;
- define and disseminate best practices for integrating research and clinical networks;
- evaluate the capacity of controlled research vocabulary resources to support integration of clinical practice and research data;
- implement interoperable and universally accessible technologies (rather than proprietary systems) for sharing Medicare claims and other data with researchers; and
- establish communication strategies for timely, appropriate data sharing with and among researchers, and to disseminate research results to health care providers and consumers.

Create “Continuous Learning” in Health Care

Dr. Rosenkrans said that HIT is the key to creating an infrastructure for a “learning health care system.” This system would constantly generate shared data on health outcomes leading to appropriate, personalized medical decisions.

To promote patient-centered CER, Dr. Rosenkrans, pointed out that stakeholders must work together in new ways and form what may seem unlikely partnerships from today’s perspectives. For example, he envisioned pharmaceutical and biotech companies working with payers like CMS, the diagnostic industry, and provider organizations to accelerate research for the genetic-based, designer therapy.

Applying Comparative Effectiveness Research

Panelists considered various ways CER can be appropriately applied.

Dr. Gottlieb discussed the options for applying CER and noted that the tendency is to try to use this information to make binary decisions. He said, “Ultimately that would be a terrible choice, because the history of all of medical evidence development, I think, shows that it’s very rare that you have a single study that really resolves an important question. More often than not, the most important questions in medicine have been resolved through a series of studies that have led to incremental additions to our ultimate thinking about a medical question.”

Drs. Wilensky, Drozda and others noted a range of potential uses of CER for making policy-level and treatment decisions. Dr. Wilensky said she envisioned use of CER in reimbursement, rather than coverage, decisions.

Panelists agreed it should be used with caution in coverage and payment policy decisions. “There’s a danger here that enforcing results with financial incentives and other bad things could end up creating problems.” Dr. Drozda observed. CER “is a valuable tool. It is how it’s used that is important, and you can’t replace clinical judgment.”

Ms. Bright considered application of CER results from the patient’s perspective by pointing out that there are currently many alarming uses of this information affecting people’s health care and their quality of life. Ms. Bright spoke about Maryland’s decision to apply the results of the CUtLASS trial, a large study comparing schizophrenia medicines, to the state’s Medicaid drug policy. “In the Maryland state budget there’s language that justifies a \$3.5 million cut to their Medicaid drug benefit program that’s entirely based on the CUtLASS study that came

out that implied that first-generation agents were better than second-generation agents for the treatment of schizophrenia. And, if we think that's good public policy or good personalization of treatment, it's really scary to come to that conclusion."

Dr. Rosenkrans expressed concern that a rigid CER standard could chill medical innovation. "Merely adding the costs of providing comparative effectiveness information onto the current trends in R&D economics, generates a decidedly bleak emerging picture whether you take a conservative or more liberal view of the costs involved."

There was also emphasis on the value of communicating the results of CER to physicians and patients to improve treatment decision-making. Dr. Drozda said he believes that one goal of CER studies should be to provide information for practitioners, because these studies offer valuable clinical decision-making input.

Several panelists stressed the importance of clearly communicating CER information to all appropriate stakeholders — patients, clinicians, and researchers. The Medicare Modernization Act Section 1013, which authorized AHRQ to conduct CER, requires the Agency to communicate research results to multiple audiences. Dr. Clancy described the AHRQ approach, which includes translating research results so patients of various literacy levels can understand them, and providing more detailed information for clinicians.

Ms. Bright asserted that patient materials need simple language and concepts to reach adult consumers who read at the 4th to 6th grade levels. Peer services have been shown to improve adherence. Therefore, involving peers in CER results translation for patients is another potential way to educate this audience.

Conclusion

Dr. Balas and Mr. Pitts concluded the conference by highlighting the issues that emerged and identifying some areas for further discussion. These included:

- identifying and supporting patient-centered approaches to CER;
- developing new mechanisms for establishing a research agenda and research questions based on patient and provider information needs;
- stronger research methods, particularly for observational research and non-randomized clinical trial designs;
- the importance of a broad scope of research that examines health system attributes beyond medical technology;
- ensuring that CER evolves in ways that support the emergence of personalized medicine and HIT; and
- clearly defining goals for government CER that are consistent with optimal patient care and improved health care quality.

Mr. Pitts raised the potential for unintended consequences and wondered if a focus on reducing costs and maintaining patient-centered care could co-exist. "We're not at the end of this debate, we're not at the beginning of the end of this debate, but I think we are at the end of the beginning where at least we can all agree that this is not, and must not, be exclusively a debate about saving money. It must be about patient care."

