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Comparative Effectiveness Research: Potential Impact on Cancer Care Quality and Access

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review

Dr. Pearson focused his remarks on the impact of comparative effectiveness research on cancer care and access. He set the stage for this discussion by noting two points: 1) more than 90% of anticancer agents approved by the Food and Drug Administration (FDA) in the last four years cost more than $20,000 for a 12-week course of treatment, and 2) providing all cancer patients one additional year of life through cetuximab would cost $440 billion.

In 1978, according to Dr. Pearson, the United States was essentially in line with other countries in the percentage of GDP spent on health care. Since that time, spending in the United States has diverged dramatically from that of other countries, with the US now spending a much greater percentage of GDP.

The health reform law places significant emphasis on comparative clinical effectiveness research, whether through evidence generation (new studies) or evidence synthesis (technology assessments). However, there are limits in the statute related to the work of the Patient-Centered Outcomes Research Institute (PCORI). The results of the work cannot include mandates for coverage or payment. Neither can a quality-adjusted life year or other cost-effectiveness threshold be used to determine coverage or payment. Comparative effectiveness research (CER) can be used as part of a larger and iterative process.

PCORI represents a different model from most comparative effectiveness research efforts. There is a requirement for patient input into the PCORI research priorities, and the PCORI Board is dedicated to giving the concept of patient input real meaning. The Board is attempting to make PCORI function less like the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health (NIH) and more like a patient-centered institute.

Among the questions considered by the PCORI board are:

- Who does the research?
- How can PCORI money be used for better patient input?
- How can patient input influence research design?
- How can patients identify the outcomes or topics of importance?
Dr. Pearson offered an international example related to epilepsy research to underscore the importance of patient input regarding research and research outcomes. In an international study, mothers of children with epilepsy criticized the traditional measure of epilepsy outcome – seizure control – and urged that this measure be modified to take into account drowsiness resulting from seizure control. This is just one example of the tendency of clinicians to frame research questions in a way that may not be meaningful to patients and families.

Dr. Pearson identified the recent study of lymph node removal in breast cancer patients as the kind of research that PCORI might help to accomplish. The lymph node study was a study that is hard to fund and not necessarily easy to undertake, but it produced research results that might immediately help patients.

Dr. Pearson also presented a multi-stakeholder approach to prostate cancer treatment education as a positive example of CER. In the prostate cancer example, a multi-stakeholder group took the data about prostate cancer treatment and created a resource center for patients. In this patient education effort, brachytherapy and IMRT were described as having comparable effectiveness, but brachytherapy was described as high value and IMRT as low value. Proton beam therapy was described as having insufficient evidence to support coverage and to be of low value. Providers used the information about prostate cancer to transform the care of their patients, and patients gave positive feedback about this approach. Payers have changed their payment practices as a result of this prostate cancer effort; they have increased payment for brachytherapy, decreased payment for IMRT and refused to cover proton beam therapy.

This was a low-risk prostate cancer information source and was unusual because the institutions decided to use one website across all institutions. There was a community standard for evidence, and it was not owned or controlled by any one institution.

Dr. Pearson, working with Dr. Peter Bach, has been looking at a model that would retain the usual threshold for coverage but would set different levels of payment based on CER results. Under this model, if the therapy is comparable to other treatments, the payment would be comparable as well. If the treatment is superior to existing treatments, the payment would be greater. If there is insufficient evidence regarding the treatment, there would be a three-year period for manufacturers and providers to develop evidence to justify payment. Dr. Pearson made clear that this model is not in the law or being seriously considered at this time, but it is being floated as a model to guide the use of evidence.

Dr. Pearson stated that if CER is perceived as a high barrier to entry for new drugs or as a damper on pricing, venture capital may look somewhere other than cancer drug development. Cancer has been one of the areas where payers have been willing to pay high prices for treatments that provide marginal improved outcomes, but CER could have an impact on that.

Overall, said Dr. Pearson, there is more promise than peril to CER and it can be a positive tool for those with cancer.

Scott Gottlieb, MD
Resident Fellow
American Enterprise Institute for Public Policy Research

Dr. Gottlieb opened with comments about comparative effectiveness research and PCORI. He said that he did not think that PCORI would have a great impact on oncology right away, in part because cancer trials are already designed in a way that makes them CER trials. In addition, PCORI does not have the resources to finance the very large, rigorous studies that would be necessary to compare cancer treatments.
Dr. Gottlieb does believe the Independent Payment Advisory Board (IPAB) will have an impact on oncology. The IPAB, despite challenges from the left and right, is likely to survive because repealing this provision of the Affordable Care Act (ACA) is accompanied by a significant budget score. Dr. Gottlieb also suggested several practices that could result from the full functioning of the IPAB, including tacit reference pricing by the Centers for Medicare & Medicaid Services (CMS) and more aggressive use of the national coverage determination process by CMS. In the case of reference pricing, CMS will price new products off existing prices and will challenge companies to bring data to prove that higher prices are justified. However, he does not believe that cancer will be the first place where CMS will attempt reference pricing. In its exercise of the national coverage process, CMS may make off-label policy the first place for challenge.

Dr. Gottlieb also suggested that the 340B drug pricing mechanism will have a significant impact on oncology drug manufacturers, as more and more oncology practices are being sold to 340B hospitals.

Dr. Gottlieb also raised a number of issues about the implementation of policies for introduction of follow-on biologics. He questioned whether the approval process for follow-on biologics will be streamlined or if it will be similar to the current BLA process. According to Dr. Gottlieb, if the Food and Drug Administration (FDA) does not find the right balance in the approval process, the follow-on biologics manufacturers will not find the pathway to be acceptable. In addition, the follow-on biologics manufacturers want to have the same generic name as the brand name, even if there is no proof that the drug can be safely interchanged.

To create a competitive market for biosimilars, said Dr. Gottlieb, it may be necessary to eliminate the artificial divide between Part D and Part B drugs. He said that the private sector is managing drug coverage and payment across all settings, and it will make sense in the future for biological and small molecules to be in the same program. Dr. Gottlieb suggested collapsing Medicare Part B and Part D drug coverage into a single system, because he thinks it is better to adjudicate coverage and payment in the private market than at CMS.

Also of concern to Dr. Gottlieb is the kind of coverage that will be available through the exchanges of the Affordable Care Act, as he thinks there will be a race to the bottom. Dr. Gottlieb asserted that the internal battle that occurred within the Obama Administration regarding the regulation of the exchanges was won by the Department of Health and Human Services, and the result will be tighter government regulation of the products offered through the exchanges.

Barbara M. Rothenberg, PhD
Associate Director
Technology Evaluation Center
Blue Cross Blue Shield Association

Dr. Rothenberg described the practice of the Blue Cross Blue Shield Technical Evaluation Center, which is to conduct evidence-based evaluations of medical practice. She described this as being much more than a matter of comparing the red pill to the green pill. Instead, it requires understanding how treatments fit into the health care system.

Dr. Rothenberg described the BCBS system of comparative effectiveness research by providing some concrete examples. In 2008, the Minnesota Evidence-based Practice Center (EPC) initiated an expert panel to identify future research needs for prostate cancer. At the beginning of the project, it was assumed that the recommendations would relate to research needed on each of the specific types of treatment. Instead, the panel shifted to a consideration of who should be treated.
A second cancer-related review was a review to determine the most effective method of radiation therapy after breast cancer surgery, an analysis for which context is critical and where it is necessary to determine the length of follow-up to compare recurrence. In this case, randomized clinical trials comparing whole breast irradiation and accelerated partial breast irradiation are ongoing and mature results are not yet available.

There are significant obstacles to CER in cancer. One of the issues of comparative effectiveness research is that it is generally limited to evaluation of cancer diagnosis or treatment and is less useful in evaluating patient-reported outcomes. However, there have been some recent exceptions to the general rule, including the recent study on palliative care in lung cancer patients. This study compared early palliative care plus standard care to standard treatment only. Some results of the study were expected, including better quality of life and better utilization of health care resources. Counter-intuitively, the provision of early palliative care also resulted in the extension of life in the research arm.

AHRQ would like to expand the range of CER topics beyond diagnosis and treatment. Cost is one of the issues that should be evaluated, because controlling health care costs is the linchpin of achieving affordability in health care. However, Dr. Rothenberg stated, health insurers should not necessarily be the ones to raise issues of cost. Instead, providers and patients should increase the focus on evaluating cost. When BCBS does its reviews, it evaluates treatments without reference to cost.

Dr. Rothenberg described CER as a means of addressing strategies to manage a condition, but the CER researcher stands on the shoulders of present knowledge, which may be shaky ground indeed.

John Santa, MD, MPH
Director
Consumer Reports Health Ratings Center

Dr. Santa said that Consumer Reports welcomes the fact that CER is part of the health care equation, as it presents a new paradigm in health care.

Dr. Santa said that a first principle of CER should be that consumers deserve to know our conflicts of interest. A second principle is that one must consider context when undertaking CER. The health care system is about money, competition, and markets. We need to start treating each other like adults by basing CER on the assumption that this is about business. It is also important to realize, says Dr. Santa, that the CER playing field is not level, as industry dominates the flow of information to consumers. Industry is spending billions in direct-to-consumer advertising and physician marketing and billions in a biased research enterprise that favors industry.

Dr. Santa described the effort to level the playing field as a daunting challenge but one that can be met. He cited several efforts to reveal conflicts of interest and provide consumers with information about the biases of researchers and health care providers. He cited the ProPublica analysis and release of financial relationships information, the Fugh Berman analysis of estrogen literature published in the PLoS, the Rothman work on health advocacy organizations and their support from the pharmaceutical industry, and the recent release of information about the St. Jude Medical, Inc.-Department of Justice agreement related to kickbacks for putting children on post-marketing trials for defibrillators marketed by St. Jude Medical.

Key consumer principles have been articulated to guide CER. Consumers should be involved from the start in CER, including in setting research priorities. There must be careful selection of both consumers and researchers in CER, and training, orientation, support, and feedback are needed for both consumers and researchers. Moreover, independence is crucial for both consumers and researchers.
Dr. Santa cited a supplements issue of *Consumer Reports* to support the proposition that consumers will use comparative effectiveness research results. That issue resulted in more visits to the site than any other story or cover. There was strong readership interest and scores for all of the health articles in that issue, and also strong media interest.

There are a number of successes in putting information into the hands of health care consumers, including clinicaltrials.gov, the Drug Effectiveness Review Project, rating charts, and decision guides. Implementation of surgical checklists in American hospitals has been more difficult.

On the horizon in terms of information and decision support for health care consumers are Medicare physician performance data, a national reporting system for hospital infections, PCORI, required reporting about physician financial relationships, and information available through the ACA exchanges.

Dr. Santa addressed cancer comparative effectiveness research opportunities with the warning that, “if you want to say yes, you must also be willing to say no.” He said that the country is in a situation where we suffer from poor delivery of what we know works and overuse of what we know does not work. To improve care, we can start with data about prevention services, diagnostic testing, and elective treatments; we should free the data and use it for comparisons.

Dr. Pearson asked Dr. Santa to comment on the policy implications of heterogeneity. How do we assess different kinds of heterogeneity? Dr. Santa said that while heterogeneity of patients is important, heterogeneity of provider performance is just as important an issue.

Dr. Pearson also said that although we think of CER as providing answers to patients, in fact CER just provides the patient the right questions to ask. Patients can “do the math for themselves” if they have the right questions to ask.

Dr. Rothenberg said that every evaluation the BCBS centers undertake is accompanied by a struggle related to demographics. Even age is poorly defined, and race is definitely poorly identified.

Dr. Santa said that Consumer Reports would like to rate genetic tests because they think that the available tests are so poor, and they note that there are serious misuses of genetic tests. Dr. Pearson said that much of this relates to decisions by manufacturers early on regarding how a drug will be tested and if it will be tested in connection with a genetic test that contributes to targeting.

Dr. Rothenberg said that we are increasingly looking at cancer studies where the impact of the new treatment is very small. But the findings of such trials do not necessarily answer the question of whether it is a few patients who got much better or all patients who enjoyed a very small benefit. Much of the time, said Dr. Rothenberg, articles on new treatments give us very little information about the data on the treatment.

The panelists were asked to comment on the efforts to include patient or consumer representatives as part of the CER process. Dr. Rothenberg said that AHRQ makes a strong effort to include patient or consumer representatives in their CER panels, although patient and consumer representatives may be considered different categories of participants in different contexts. Dr. Pearson said that the PCORI board is serious about inclusion of patients in their process.
Ms. Pollitz provided an overview of the provisions of the Affordable Care Act (ACA) that offer important protections to cancer patients, including but not limited to the Pre-Existing Condition Insurance Plan, coverage for dependent children to age 26, consumer protections in insurance, and rights of appeal.

According to Ms. Pollitz, accountability and affordability in the health insurance market are fundamental goals of the ACA. As one example of the effort to realize these goals, she highlighted the issuance of regulations that provide for public review of rate increases. The federal government will rely on the states for the first round of rate review, but if states do not have an aggressive enough or competent rate review, the federal government will assume rate review responsibilities. She offered the case of BCBS California, which proposed rate increases that they are now backing away from after questions from the federal government, as an example of the exercise of this federal authority.

Ms. Pollitz discussed briefly the mission of her office within OCIIO, which is to make the insurance market friendlier to consumers by providing them more complete and comprehensive information about insurance choices. She then turned her attention to the work on the implementation of the insurance exchanges. Of fundamental importance in the exchanges, which may reach as many as 99 million Americans, is the collection of data about what is happening to consumers and the constant feedback of information to improve the exchange system.

Ms. Pollitz detailed the coverage information that will be available to consumers via the website, www.healthcare.gov, including information regarding the Pre-Existing Condition Insurance Program, COBRA, Medicaid, and private insurance options. The data on the website will include information on the individual health insurance market, such as information about coverage and cost.

When the Department of Health and Human Services (HHS) launched the website of insurance information, it received a Freedom of Information Act (FOIA) request. The ruling on that FOIA request has just been released, and according to that decision HHS will make all of the data underlying the website public. This FOIA determination will allow consumers to review rate and other data and use it as they see fit, according to Ms. Pollitz.

According to Ms. Pollitz, the Department is not looking back or fighting battles about enactment of the Affordable Care Act. Instead, they are looking forward toward the monumental task of implementation. This requires identifying partners, accepting suggestions of ways to do things better, and choosing flexible approaches to solving problems.

Ms. Pollitz was asked to comment on what action would be taken in those states that do not undertake to administer their own exchanges; she said that it was hard to forecast at this point how many states will not choose to administer their exchanges. She said that HHS was separating what was happening at the political level – the legal challenges of the Affordable Care Act – from what is happening on the practical level – the efforts by the states to implement the ACA. At the time of the meeting, Alaska was the only state that has not applied for any money to implement its exchange; HHS is working with partners in every other state. Most states have also made clear that they intend to use www.healthcare.gov as the beginning of their information system.
Ms. Pollitz was asked to comment on the use of interim final rules instead of notice-and-comment rulemaking for many elements of the ACA. She noted that the government is allowed to rely on interim final rules when it is facing an imminent deadline, will modify interim final rules when necessary, and will utilize notice-and-comment rulemaking whenever possible.

Ms. Pollitz responded to questions about the grant of waivers in the case of medical loss ratio requirements. She offered the example of the state of Maine, where the insurance commissioner has applied for a slower phase-in of the MLR requirements. HHS is entertaining the request from Maine, a state with only two carriers in the individual marketplace, to allow them to comply with MLR requirements by 2014.

Dan Durham  
Executive Vice President  
Policy and Regulatory Affairs  
America’s Health Insurance Plans

Mr. Durham identified several key obstacles to implementation of the ACA. He said that the individual mandate is critical to the smooth working of the insurance market reforms, and the challenge to the mandate in the courts creates some uncertainty about the implementation of ACA. He noted that achieving a balance of coverage and affordability will also be difficult for HHS.

He cited the relationship of increases in the cost of essential benefits and government subsidy costs. A ten percent increase in the cost of essential benefits will boost government subsidy costs by a hefty 14.5 percent. In 2014, there will be a number of additional issues related to ACA implementation. Premium taxes may increase premiums by as much as 3%, or $5000, over a decade. Beginning in 2014, premiums can only be adjusted according to age at a rate of 3 to 1. Most states currently permit 5 to 1 or even 6 to 1 age rating. Immediate compression of age rating in 2014 might increase premiums by as much as 30%. There is also the fact, according to Mr. Durham, that underlying medical costs will be increasing. If premiums go up rapidly, as may be the case, it is also possible that younger and healthier individuals will pay the penalty instead of purchasing insurance.

Mr. Durham recommended the elimination of the ACA tax on premiums and adoption of a more reasonable rule on age rating, along with a continued focus on the elimination of cost-shifting. These actions will control costs and therefore help to control premium increases.

Mr. Durham also described centers of excellence, which focus on networks of providers to boost quality of care and patient satisfaction, as important to cost control. He noted that they may be especially important in cancer care and management.

Otis Brawley, MD  
Chief Medical and Scientific Officer  
American Cancer Society

Dr. Brawley began his remarks with the challenge that we need to transform health care. He said that he and his colleagues at the American Cancer Society (ACS) want to keep people focused on making the ACA work and then moving beyond it. One signal of the ACS commitment to the ACA is the organization’s support for an amicus brief supporting the constitutionality of the law.
He described the necessary transformation of the health care system as a movement to a health promotion system. He said that there are three fundamental issues confronting US health care: ignorance, apathy, and greed. He suggested that transforming American health care will require reducing costs, decreasing disparities, and improving quality of care. Dr. Brawley urged an understanding of the scientific method, as a first step toward an evidence-based system of prevention and care. Such a system is one that ensures the rational use of medicine and not the rationing of medical care.

Dr. Brawley emphasized that access to insurance does matter. One only need look at the relationship of insurance coverage and colorectal cancer survival to see the importance of coverage. However, within a system of coverage of all, there is still a need to address the issue of over-consumption of health care, or medical gluttony.

He described overutilization as a multi-level problem: 1) patients who believe in cost containment until you are talking about them as the patient, 2) doctors who are paid to treat, 3) hospitals and clinics that are paid to treat, and 4) insurance as a big business. He also identified the elements of so-called medical gluttony as screening tests of no proven value, treatments of no proven value, and laboratory and radiologic imaging done for convenience.

Of critical concern to Dr. Brawley are the effects of obesity on the health care system. He identified the rates of diabetes, cardiovascular disease, orthopedic injury, and cancer as linked to obesity, high caloric intake, and lack of physical activity. Unless we address the crisis of obesity, he said, health care costs will continue to escalate.

Stuart Butler, Ph.D.
Distinguished Fellow and Director
Center for Policy Innovation
The Heritage Foundation

Dr. Butler began his remarks with the assumption that any effort to derail the Affordable Care Act (ACA) will be unsuccessful. With that assumption in mind, Dr. Butler commented on the enormity of the task of implementation of the ACA, which affects one-sixth of the US economy. He said that this fact – the significant economic impact of the ACA – should be remembered as the implementation process moves forward.

Dr. Butler said that there will be significant uncertainties about the interpretation of the ACA and how the health care system will respond to the ACA. He suggested that we are already seeing some of this uncertainty at the state level, with states seeing contradictions or complexity in the Medicaid provisions of the law. States facing serious budget shortfalls are seeking creative ways to interpret the legislation, including by trying to direct residents to the exchanges and away from Medicaid.

He also said that employers will be trying very hard to put employees in the exchanges, as Mr. Durham also suggested. Efforts by the states to interpret the legislation to reduce their costs and actions by employers to shift employees to the exchanges will both result in increased federal costs for the ACA. This will in turn prompt a re-examination of the legislation to reduce its overall cost.

Dr. Butler also identified the Independent Payment Advisory Board (IPAB) as a big problem in the ACA. The IPAB has the fundamental function of ratcheting down the cost of the Medicare system, and he predicts that the result will be a ratcheting down of payments to providers and subsequent effects on access to care.

Dr. Butler also noted that there is still the large outstanding task of defining essential benefits for plans offered through ACA exchanges.
Karen Davenport  
Research Project Director  
Department of Health Policy  
George Washington University

Ms. Davenport said that she would use Dr. Brawley’s remarks about the need to transform the health care system as a point of departure for a review of coordination of care across providers. She said that the ACA provides significant opportunities – whether in the accountable care organization (ACO) regulations or in other demonstration projects or other tests – for encouraging and incentivizing providers to coordinate care and employ case management techniques. One example of this is the reduction of reimbursement for hospital readmissions.

Ms. Davenport also identified dual eligibles as patients who should be special targets for case management and care coordination. These individuals are among the most expensive in the health care system and they are receiving fragmented care instead of receiving the very best of Medicare and Medicaid.

She also suggested that major changes to the health care system are possible, and those will be changes to Medicare and Medicaid that occur outside the context of ACA implementation. She predicted that Medicare and Medicaid changes are possible as a result of budget debates and compromises.

Ms. Davenport identified the definition of essential health benefits as an area where there are opportunities for advocacy at both the state and federal levels.

**Prescription Drug User Fee Act: How Will Cancer Drug Development and Review be Affected by the Reauthorization?**

James Greenwood  
CEO  
Biotechnology Industry Organization

Mr. Greenwood began with a description of the drug development process. He said that the development of a new drug takes 11 years and costs $1.2 billion. He attributed part of the length and cost of therapeutic development to the extension of the length of the average drug review process. The average length of the FDA review process is now 780 days for a new drug.

He noted that BIO companies and investors are working to develop a new generation of therapies, but this will take a strong and reliable science-driven regulatory environment. FDA has struggled to meet its mission with inadequate funds. Congress has in recent years failed to appropriate funds, and industry interests must rely on the Prescription Drug User Fee Act (PDUFA) to reverse this trend.

The industry goals in the PDUFA reauthorization process in 2012 are straightforward: 1) a clear and predictable review process, 2) a return to the basics at FDA, meaning an emphasis on the essential health mission of the agency, and 3) promotion of scientific dialogue and transparency.

To ensure more reviews that are “on time,” industry and the agency have been discussing a new review module that incorporates more communication and transparency. There has also been discussion of ways to strengthen the regulatory science capability of FDA.
The review of rare disease products has attracted special attention during industry-agency discussions. There is agreement that there should be more training of FDA staff and consultants for rare disease product review and that there must be more structured discussion related to rare disease product review.

There is also an acknowledgement that there must be an enhanced use of information technology to support the electronic submission of applications. The information technology must be standardized so there is predictability for companies.

Unmet medical needs for rare diseases may best be met by small companies. However, the current procedures of FDA may present special challenges for small companies. Tough science issues need to be raised early in the process and be addressed at that time. This may be especially important for small companies. When questions arise early on, the company wants to get in touch with FDA scientists to achieve resolution of difficult issues. FDA currently relies on a formal approach with 30-day response windows. This process results in ping-pong communication that is difficult for all companies but perhaps cost-prohibitive for small companies.

Technical discussions between industry and the agency will be completed by mid-April 2011, with January 2012 the target for an agreement between FDA and industry. Mr. Greenwood also noted that, while the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act are not part of the core PDUFA provisions, they may be considered at the same time as PDUFA.

Mr. Greenwood offered a caution about PDUFA. He noted that PDUFA also addresses the matter of resources available to FDA, but it will not address many issues related to drug development.

Mr. Greenwood said that biotechnology companies face challenges, as science is better than ever. He said that BIO has hired the consulting firm of Elias Zerhouni to identify “wild” ideas for the reinvention of the research and development process and the regulatory process. According to Mr. Greenwood, BIO asked Dr. Zerhouni and his group NOT to exclude any idea because it might be perceived as risky or politically difficult. BIO will vet Dr. Zerhouni’s ideas by June 2011 and based on those ideas will develop a bill addresses capital formation, regulatory issues, reimbursement matters, and other issues affecting drug development. This will be a “thought piece” that will address tax policy and incentives for unmet medical priorities and diseases with a heavy burden. Among the approaches under consideration are a DARPA-like plan for drug development, adaptive trial design, and creating a national culture of innovation.

Mr. Greenwood also commented on the lack of understanding about the full continuum of drug development among some policymakers. He said that too many think they can fight biotechnology companies on reimbursement for innovative products and still have a steady supply of new drugs.

Mr. Greenwood also cautioned that the cost of care for the baby boom generation is unsustainable and urged greater investment in disease prevention.

In response to a question about the National Institutes of Health proposal for a National Center for Advancing Translational Science, Mr. Greenwood said that the NIH concept would only work if NIH and industry collaborate. One of the ideas that Mr. Greenwood has been considering is a process in which industry identifies basic science questions that are confounding the companies and slowing drug development and presents those questions to NIH for investigation in NIH-funded projects undertaken by intramural and extramural researchers. NIH could maintain a list of the projects presented to the agency by industry and accept applications on these questions. This process would advance science in a very clear way.

Another participant asked Mr. Greenwood about strategies or policies to encourage companies to collaborate in the pre-competitive space, collaborations that may be necessary to test combinations of drugs that are especially necessary in cancer treatment. He said that more and more companies are sharing data, and this
process is making all of the participants smarter. He said that BIO is a big fan of this collaborative approach and will consider including it in the big ideas package.

Mr. Greenwood, in response to a question about the Medicare national coverage determination for Provenge, said that the agency is going to a space where it should not be.

**Quality Cancer Care: Initiatives to Reform Care Delivery and Payment**

*Daniel Hayes, MD*

*American Society of Clinical Oncology*

Dr. Hayes described the American Society of Clinical Oncology (ASCO) Quality Oncology Practice Initiative (QOPI) as a program that creates a culture of self-examination and evaluation in oncology practices. QOPI involves retrospective chart abstraction, accomplished twice a year, and data analyses and confidential practice reporting.

There are now more than 990 practice sites – small, large, institutional, and academic – participating in QOPI. Measures are developed by a QOPI steering committee, assisted by the ASCO staff, and grounded in the work of the various committees of ASCO, including the quality of care, clinical practice, and guidelines committees. The measures utilized in QOPI are both evidence-based and consensus-based. The QOPI measures include: 1) a set of core measures that include documentation of care, chemotherapy planning, administration, and treatment summary, 2) disease modules that relate to the management of specific types of cancer (breast, colon, non-small cell lung cancer, etc.), and 3) domain modules, like those addressing care at the end of life and symptom/toxicity management.

QOPI is recognized in other forums and systems as well; QOPI serves as an American Board for Internal Medicine standard and can be used to earn continuing medical education credits.

ASCO is considering ways to make the QOPI system even more dynamic by attaching a registry to it. This kind of development would create a rapid learning system of databases that include large numbers of events linked in a way to support decision-making and permit rapid and powerful analysis of outcomes and cost. The organization is attempting to coordinate three quality programs: 1) guidelines, 2) performance measures, like QOPI, and 3) health information technology. The coordination would represent movement toward a rapid learning system.

*Russell Hoverman, MD, PhD*

*Texas Oncology*

Dr. Hoverman began his remarks about quality improvement initiatives with a reminder that the judge of the relative value of a medical intervention is first and foremost the patient. And the patient will make the decision about value on the basis of both empiric and subjective evidence.

Dr. Hoverman identified a long list of obstacles to quality health care delivery, ranging from having to wait too long for an appointment to lack of insurance coverage to lost time at work to wrong treatment.

He described initiatives of Texas Oncology that are intended to address the obstacles to quality care. In 2004, a Practice Quality and Efficiency (PQE) program was implemented; in 2005 the QOPI program described by Dr. Hayes, was put in place; in 2005 a pathway program for medical oncology and hematology that evaluates evidence, toxicity and cost to the patient of all treatments was initiated; and in 2009 an effort that combines
pathways with a telephonic call system, support for self-management of chemotherapy, and advance care planning was established.

The pathway approach is a three-phase approach: 1) an evaluation of the clinical evidence for comparable drugs, 2) a comparison of the toxicity profiles of the drugs, and 3) a choice of the least costly drug as the on-pathway option, if the drugs are clinically equivalent. In this system, pathways are reviewed on a quarterly basis, and ASCO and ASH publications are reviewed immediately and their recommendations incorporated.

According to Dr. Hoverman, if pathways are to be utilized, we must be sure that outcomes are no worse than if pathways were NOT used. He cited the Virginia Mason back pain program, in which processes were revamped. In the new system, a person with back pain sees a physical therapist before an MRI, as compared to the previous system where the patient received the MRI initially. In the revised system, MRI use dropped significantly, and the institution lost $200 per case compared to previous practice. This is an issue for institutions that initiate programs to reduce costs. Do those institutions get a share in the savings? In the case of the Virginia Mason program, the institution addressed this issue by negotiating for increased payments for physical therapy services. The other option for institutions is to replace lost revenues by increasing volume.

The pathways approach has much potential, as it integrates medical, radiation, and surgical oncology services. There is the potential for including advance care planning in the pathways, but this is the toughest service to integrate, as oncologists were not trained to do advance care planning. End-of-life discussions are difficult, as they are accompanied by high patient and family anxiety.

Dr. Hoverman also said this is a time of great uncertainty in cancer care, with a lack of clarity about how things will be in five years. This level of uncertainty essentially creates a headwind working against a pathways approach. The national average practice size is 3 to 4. Median oncology practice income has dropped. The average oncologist is seeing more new patients. Most practices are single specialty. And software platforms do not talk to each other. Overall, the challenges to oncology practice are significant, and as a result, the obstacles to implementing a pathways program are also substantial.

William McGivney, PhD
CEO
National Comprehensive Cancer Network

According to Dr. McGivney, he wrote his presentation right after being on Capitol Hill, where he was struck by the preoccupation with the Affordable Care Act to the exclusion of other matters. Dr. McGivney offered the caution that this preoccupation may be resulting in an abandonment of cancer care quality activities that worked in the past. Specifically, he mentioned the 2006 oncology quality demonstration project, developed by ASCO and NCCS in collaboration with Peter Bach of CMS under significant time pressure. The process of developing the oncology quality program began at Thanksgiving 2005, and the initiative was operational by mid-January 2006. The system, based on NCCN decision guidelines related to 14 tumor types, was an effective means of improving cancer care quality.

In 2008, United Healthcare announced that it would cover all drugs in the NCCN compendium. Aetna and WellPoint have implemented variations on the United HealthCare plan. This system works well, with the potential for developing a summary of treatment from the NCCN guidelines.

Another current and ongoing NCCN projects is the development of a comparative effectiveness therapeutic index.
All of the examples offered by Dr. McGivney were intended to underscore the fact that a number of cancer quality improvement efforts have been undertaken in the last decade, with none of them dependent on the Affordable Care Act. Innovation and quality improvement have been underway in the cancer community for quite some time.

Mandy Cohen, MD  
Center for Medicare & Medicaid Innovation

Dr. Cohen introduced herself as a primary care physician currently serving as a senior advisor at the Innovation Center, established by the Affordable Care Act to test payment and care delivery models in Medicare, Medicaid, and SCHIP. The Center became operational in November 2010. She said that the employees of the Innovation Center are essentially doing what folks in a start-up do: creating the entity and its structure.

The Innovation Center is considering various patient care models that focus on patients getting the right care at the right time in the right setting all of the time. Care must be safe, reliable, and timely. One “big bucket” for innovation is accountable care organizations, or ACOs. The Innovation Center will also look at initiatives to create medical homes and to establish systems of bundled payments.

According to Dr. Cohen, there is much work to be done. The Innovation Center is gathering ideas related to payment models that have worked across the country and should be further tested. The selection of models will be completed through a competitive process. The Innovation Center is looking for projects in the private sector that have improved quality and reduced cost.

The Center for Medicare & Medicaid Innovation will scale up and expand the models that work. CMMI has $10 billion over ten years to do its work. This amount is obviously not enough to do everything the center wants to do, and as a result the Innovation Center is pursuing partners in the private sector to accomplish its work.

Dr. Cohen noted that the Stark and anti-trust laws have limited Medicare demonstrations in the past, but the ACA demonstrations are not fully subject to those laws. Moreover, if the CMS actuary certifies that demonstrations save money, CMS can move forward to expand them without going back to Congress for authorization to expand.

Dr. Cohen was asked to comment on the assertion of some in the cancer community that there are few at CMMI or CMS who have expertise in cancer care. Dr. Cohen said that CMMI is building a phenomenal team with expertise in many therapeutic areas. She predicted that the cancer community will be pleased with the team that is being developed and that they will find they have champions at CMMI. However, she noted that partnerships with specialty colleagues outside the CMMI will be absolutely critical to advance the center’s work.

Dr. Cohen was also asked to comment on the strategy that CMMI and CMS would employ to replicate successful demonstration projects. She reiterated that a project that improves quality and reduces expenditures can be expanded on a regional or national level without Congressional review and approval.

A participant asked Dr. Cohen to define the timeline for savings. If a demonstration project did not produce savings in its first or second year but would produce savings in the third year and after, for example, would it be approved by CMMI? Dr. Cohen said that there is an ongoing discussion about the definition of “savings.” She admitted that there was an emphasis at the present on projects that produce savings in the shorter term.

Dr. Cohen noted that the accountable care organization (ACO) proposed regulations would be issued soon, and she said only that CMMI hopes to see tests of different types of payment systems in ACOs.
She also noted the significant interest in addressing the dual eligible population, which has great needs and is also very costly to care for. Dr. Cohen said that there has been some focus on models for bundled payment, but it is unclear how those models will be designed or proceed.

Lisa Latts, MD, MSPH, FACP
Vice President, Public Health Policy
WellPoint

Dr. Latts defined the payment innovation efforts of WellPoint, stressing that these efforts were not related only to oncology. Dr. Latts emphasized the need to change the conversation that happens in our health care system, and it may be necessary to change the way we pay for care to ensure that the right conversation happens.

Of great interest to Dr. Latts and WellPoint are registries. She defined some fundamental principles to guide the use of data in registries. The data collection needs to be prospective and systematic. She noted the collaboration with cardiology colleagues to use data in payment reform efforts. She said that collection and use of data had contributed to the decrease of cardiac complications over time, an example of investing in information in order to accomplish improvements in care.

WellPoint is the parent of 14 BlueCross BlueShield entities. If WellPoint wishes to do something nationwide, it undertakes such projects with its Blues partners. There is an ongoing effort at quality improvement, undertaken through the Blues partners, that focuses in part on rare complex cancers, which are those cancers that require complex multi-disciplinary care. These cancers are not low-cost in terms of the contracted rate for care, but when complications and readmissions are taken into consideration, the new system of care and payment saves money.

She described the Blue Distinction Centers program as focusing on rare and complex cancers that involve complex surgical, radiosurgical, chemoradiation, and interventional treatments.

Dr. Latts identified significant gaps in even the best systems of cancer care, including:

- Only 28% provide written interdisciplinary treatment plans
- Only 28% can state that all radiation oncology facilities are accredited
- Only 44% can state that the medical oncology practices participate in QOPI

She also described other quality improvement efforts undertaken by WellPoint, including both accountable care organizations and bundled payment efforts. She said that, in situations where there are adequate data systems, along with the administrative wherewithal and patients to support ACOs, that model can work. However, she expressed concerns that in many situations there are not adequate systems and support for ACOs to succeed.

WellPoint is very interested in bundled payment efforts, defined as a procedure and a specified period and scope of follow-up care. The bundled payment system has the potential to eliminate bad incentives. The immediate focus for development of bundled payments for WellPoint is high-cost, high-volume procedures.

An ideal bundled, according to Dr. Latts, should target a common and costly procedure, cover essential clinical items and services, improve quality of care, provide a financial incentive to reduce unnecessary care, yield a “win-win-win” outcome for WellPoint, providers and members, be simple enough to administer effectively, and appear seamless to policyholders.
March 22, 2011

Updates from the National Institutes of Health and Food and Drug Administration

Kathy Hudson, PhD
Deputy Director
National Institutes of Health

Dr. Hudson described the philosophy of National Institutes of Health (NIH) Director Francis Collins as one of disruptive innovation, a significant shift for a place like NIH that has been very resistant to change. In some ways, that has been a good attribute, as it has permitted the agency to support researchers and advance knowledge. However, the NIH Director would like to honor the mission of NIH to support science toward better understanding and also encourage NIH to apply the science to improve health care.

After enjoying years of large increases in funding, NIH is now looking at flat budgets. NIH, like other federal agencies, is living in several budget years as Congress attempts to finalize FY 2011 funding and proceed to consideration of the FY 2012 budget and appropriations bills. The House-passed HR 1 would reduce NIH funding by $1.63 billion, or 5.2 percent below FY 2010 levels. The reduction in funding would be made across all institutes and centers at NIH. However, because the bill also calls on NIH to support a fixed number of new and competing research grants, the agency would be forced to make reductions in the funding available to existing grantees.

While NIH plays a pivotal role in supporting basic research and is known to most for this role, NIH can also make an important contribution to therapeutic development. Despite the investment of NIH and the significant investment of industry, a “valley of death” still exists for therapeutic development, a valley from which most candidate compounds never emerge.

NIH leaders have been asking what they might do to improve the success rate for compounds in testing. NIH can help through a number of programs that stretch across the entire development spectrum. The most concrete idea is one that has been approved by the Scientific Management Review Board. This group was asked by Dr. Collins to provide some advice about the role of the NIH in translational research, and in December 2010 the group unanimously endorsed a recommendation to establish a translational research center at NIH. This concept, the National Center to Advance Translational Science (NCATS), was mentioned in the FY 2012 budget request, and NIH is now working on the details to be sent to the Hill.

The intention of this center is to catalyze the development of novel therapeutics and advance translational science. The center will view the drug development pipeline as a scientific problem ripe for experimentation and process engineering. The functions of NCATS will be to experiment with innovative approaches along the pipeline, choose compelling products, and catalyze novel diagnostics and therapeutics. The center will utilize high throughput screening, evaluate animal models in collaboration with FDA and industry, and complement but not duplicate the translational research already underway.

A recent New York Times article hinted that NCATS would be a small pharmaceutical company, but that is not an accurate description. Instead, NCATS will complement and will not compete with the private sector, including industry, academic partners, advocacy groups, and other non-profits.

Dr. Hudson identified the programs that will probably be included in NCATS, including the molecular library of NIH, the Therapeutics Research and Development (TRND) program, the Office of Rare Disease Research, RAPID, and Cures Acceleration Network (CAN).
Dr. Hudson was asked by a participant to identify the greatest challenge to NIH if there are budget cuts. She said that all NIH institutes have already modeled difficult funding scenarios. The greatest challenge is ensuring that those who have just received awards are treated fairly.

Dr. Hudson said that the institutes at NIH were being asked to take a close look at their portfolios in order to eliminate any duplication of effort. They are also being asked to ensure that they are not unnecessarily duplicating or repeating work that is underway in the private sector.

Richard Pazdur, MD
Director
Office of Oncology Drug Products
Food and Drug Administration

Dr. Pazdur cited the article in the *Journal of the National Cancer Institute* that summarizes accelerated approvals of cancer drugs. Dr. Pazdur summarized the accelerated approval process and reiterated that it is inherent in the accelerated approval process that confirmatory trials must be completed to demonstrate clinical benefit.

The Oncologic Drugs Advisory Committee (ODAC) meeting of February 8, 2011, was intended to review the timeliness of the completion of studies that confirm clinical benefit. Dr. Pazdur said that the standard is that confirmatory studies are usually underway at the time of approval. In addition, studies must be completed with due diligence.

Dr. Pazdur said that his definition of due diligence is that the same resources that were dedicated to the initial approval should also be dedicated to post-marketing requirements. At ODAC meetings, sponsors have been advised to look at the accelerated approval process as a comprehensive drug development program.

According to Dr. Pazdur, there is a misconception that accelerated approval is an incentive program for the pharmaceutical industry. Instead, it is an incentive program to get drugs that are better than available therapy onto the market soon. The accelerated approval regulation makes clear that the new therapy must be better than available therapy. The standard is not one that permits sponsors to do the least possible to achieve drug approval.

The accelerated approval regulation is a patient-centered approach to drug development intended to get drugs to patients sooner. In keeping with this fundamental goal of getting drugs to patients sooner, the FDA expects that some of the drugs approved on an accelerated basis will fail their post-marketing trials. The agency expects that there will be some drugs that will not meet their primary endpoint.

When drugs do not meet their endpoints, it is not an indictment of the accelerated approval program. If the agency does not have drugs coming off the market, it is not exercising flexibility in accelerated approval. Forty drugs or indications have been approved on an accelerated basis, and 10% have been removed from the market (or the indication has been removed). This is an acceptable risk of 10%.

Dr. Pazdur also commented on the communication between EMEA and FDA. There is a representative of the EMEA at ODAC meetings at which post-marketing obligations for accelerated approval drugs are reviewed. The EMEA conditional approval program is similar to the accelerated approval process in the US. One difference is that the EMEA program is renewed on a yearly basis, with the regulatory agency reviewing the accelerated approvals on an annual basis to determine if the sponsors are fulfilling their obligations in timely fashion. Unlike in the US, the EU program of conditional approval is only for new molecular entities, with no such approval for supplemental indications. There is some interest in addressing the issue of supplemental indications in the EMEA.
Dr. Pazdur also cited tensions between companies and cooperative groups about their roles in the completion of confirmatory trials, but he stated simply that commercial sponsors are responsible for completion of confirmatory trials.

Dr. Pazdur was asked to comment on the need for a diverse population to be enrolled in a clinical trial. He said that sponsors are increasingly interested in international studies. He cautioned that pharmaceutical companies have to be aware that they need diverse populations in their trials that are representative of the populations of the countries in which they seek approval.