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With $1.1 Billion At Stake, Cancer Groups Mull "Comparative Effectiveness" Studies

By Paul Goldberg

As the federal government prepares to turn loose $1.1 billion in new funds on "comparative effectiveness research," definitions of these methods of comparing therapies seem to be elusive.

How will the government set priorities for comparative effectiveness studies? How will comparative effectiveness studies correlate with oncology studies that are focused on efficacy? What will be the required standards of evidence? How will the link between payment and evidence be established? How will cost and benefits of treatments be assessed?

In oncology, a specialty where reliance on rigorous studies coexists with the tradition of flying by the seat of the pants, the government's new

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In the Cancer Centers:

M.D. Anderson And Banner Health Plan Cancer Center in Phoenix To Open In 2011

M.D. ANDERSON CANCER CENTER and the Banner Health hospital system said they plan to create the M. D. Anderson Banner Cancer Center in Phoenix, Ariz. Located on the campus of Banner Gateway Medical Center, the M. D. Anderson Banner Cancer Center is scheduled to open late in 2011 and will be anchored by a 120,000-square-foot cancer outpatient center and supported by 76 patient beds on two floors inside of Banner Gateway. Services will include medical oncology, radiation oncology, surgical oncology, pathology, laboratory, diagnostic imaging, as well as other supportive clinical services. The anticipated groundbreaking is late 2009 or early 2010. The center will be modeled after M. D. Anderson's Houston outpatient clinics that feature individual areas for specific cancers. This center represents a $90 million project that will be funded by nonprofit Banner Health through bonds. The M. D. Anderson Banner Cancer Center represents M. D. Anderson's most comprehensive extension of its patient care outside of Houston. . . . **HARRY BEAR**, a physician-researcher with Virginia Commonwealth University Massey Cancer Center, received the Distinguished Investigator Lifetime Achievement Award from the NSABP Foundation Inc., which provides support to the National Surgical Adjuvant Breast & Bowel project, an NCI clinical trials cooperative group. During the past two decades, Bear, a researcher and surgeon, has led international trials that have resulted in major changes in the treatment of breast cancer and dramatically

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Report Provides A Thesaurus Of Comparative Effectiveness

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agenda is causing considerable anxiety.

Last week, all major cancer groups signed on to a thick and not obviously politically controversial report that lays out the role comparative effectiveness might play in oncology. The report's authors agree that signing on to the report is akin to expressing support for Roget's International Thesaurus of English Words and Phrases.

"The intention was to create a document would try to articulate the many types of research that could be considered comparative effectiveness, a Thesaurus of comparative effectiveness," said H. Kim Lyerly, director of Duke Comprehensive Cancer Center and co-chairman of the committee that compiled the report.

The document is posted by its sponsoring group, Friends of Cancer Research, at www.FOCR.org, and an excerpted version of its recommendations appears on page 5. The document was endorsed by 25 groups, including the American Society of Clinical Oncology, the American Association for Cancer Research, and the American Cancer Society.

Ultimately, the document points out that, politics aside, the hierarchy of evidence remains unchanged. "I've encountered 20 definitions of comparative effectiveness, depending on whom you ask, and I am just as confused as the next guy," Lyerly said in an interview. "Comparative effectiveness spans a spectrum of research," from dataset mining to subset analyses to observational studies to randomized controlled trials. "The intent was to remind people that the rules of evidence haven't been repealed."

At this stage, the rules of the game are being drawn up for all of medicine rather than oncology.

The most important event in defining comparative effectiveness and setting the research agenda is expected to occur on June 30, when the Institute of Medicine publishes a Congressionally mandated report that is expected to contain funding priorities. Until that report is out, NIH and the Agency for Healthcare Research and Quality will not dispense any of the funds allocated under the American Recovery and Reinvestment Act.

NIH is developing a strategy for awarding the new funds, and—perhaps just as importantly—methods for automated classification of projects that could be defined as comparative effectiveness.

This is likely to be politically charged, as NIH and NCI have wrangled about this approach to classification of cancer studies. Also, all institutes are going through their portfolios to determine whether their any of their existing programs could be classified as comparative effectiveness research and funded with stimulus money. This reclassification could free additional resources within NIH.

The committee defining the comparative effectiveness agenda at NIH is headed by Richard Hodes, director of the National Institute of Aging, and Elizabeth Nabel, director of the Heart, Lung and Blood Institute. NCI Director John Niederhuber is a member of the committee.

"We, as oncologists want to be at the table when CER issues are discussed and funded since we believe we can have very positive feedback about critical issues," said Al Benson, co-chairman of the group that produced the FOCR report, professor of Hematology/Oncology and associate director, clinical investigations at Northwestern University Robert H. Lurie Comprehensive Cancer Center.

"Building an informatics infrastructure that can communicate across databases could be a valuable use of resources, particularly if such includes information about developing technologies such as imaging and biomarkers that have the potential to better inform about individual patient treatment selection and treatment efficacy," Benson said. "It must be understood that oncology is moving toward selection of treatments based on human tumor biology, which is consistent with the observations that cancers represent heterogeneous collections of tumor cells with variations in biologic

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pathways.

"Comparative effectiveness research will therefore have to evolve over time to incorporate the informatics communication systems and the integration of individual patient factors to include human tumor biologic data and more accurate measures of efficacy through novel imaging techniques, for example," Benson said. "This is an essential message we feel must be conveyed to those who are setting policy and determining funding of individual projects."

One of the key distinctions in these programs revolves around the distinction between effectiveness and efficacy. Efficacy is determined within specific populations under controlled conditions. Effectiveness is closer to what actually happens in the real world.

While the distinction efficacy and effectiveness is clear in the extreme cases, the fine line separating one from the other may not be clear at all. Donald Berry, head of the Division of Quantitative Sciences at M.D. Anderson Cancer Center and a member of the committee consulted in preparation of the FOCR report, said he doubts whether it's possible to attempt studies to measure effectiveness.

"Effectiveness refers to benefit in ordinary clinical practice," Berry said. "We don't randomize in ordinary clinical practice. We know that patients who agree to be randomized are not 'ordinary,' and in fact that's the standard dig against 'efficacy trials.'

"There are biases any time a patient or her or his physician chooses treatment," Berry said. "One of the few circumstances in which legitimate inferences may be possible in a non-randomized setting is a retrospective biomarker study. If the biomarker was not known at the time of treatment, and if the biomarker is not highly correlated with observable patient characteristics, then treatment assignment was quasi-randomized as regards conclusions about the biomarker-defined subsets.

"If we are talking clinical trials, the distinction between efficacy and effectiveness may be illusory," he said.

The closest clinical trialists could come to answering the effectiveness question would be in "big, simple trials, where you try to construct a trial that would be as close to the way things might go in clinical practice as possible," said Richard Schilsky, president of the American Society of Clinical Oncology, chairman of the Cancer and Leukemia Group B and associate dean for clinical research at the University of Chicago.

Cooperative groups, being publicly funded, may be best positioned to conduct such studies, Schilsky said. However, this research agenda may conflict with the groups' mission to advance science.

"Where it could get interesting, though, is if we begin to build in biospecimens and biomarkers," Schilsky said. A Q&A with Schilsky appears on page 3.

"There is a lot of money that people are trying to figure out the best way to spend," said Jeff Allen, executive director of FOCR. "What this report does is talk about how, looking from an infrastructure standpoint, we can leverage these resources to create a better system that routinely creates data on outcomes as a byproduct."

In addition to ASCO and AACR, the FOCR recommendations are supported by the American Cancer Society, Association of American Cancer Institutes, National Coalition for Cancer Research, Susan G. Komen for the Cure, Lance Armstrong Foundation, National Comprehensive Cancer Network, Leukemia & Lymphoma Society, FasterCures, Ovarian Cancer National Alliance, Marti Nelson Cancer Foundation, C3: Colorectal Cancer Coalition, Men's Health Network, Inter Cultural Cancer Council Caucus, National Lung Cancer Partnership, Lung Cancer Alliance, National Patient Advocate Foundation, Prevent Cancer Foundation, The Wellness Community, Sarcoma Foundation of America, Society for Women's Health Research, Alliance for Aging Research, Autism Society of America, and National Alliance on Mental Illness.

Cooperative Groups' Dilemma: CER vs Advancing Science

The Cancer Letter asked Richard Schilsky, president of the American Society of Clinical Oncology, chairman of the Cancer and Leukemia Group B and associate dean for clinical research at the University of Chicago, to discuss potential implications of comparative effectiveness research.

The interview was conducted by editor Paul Goldberg.

SCHILSKY: Part of the problem is that nobody really knows what they are talking about when they talk about comparative effectiveness research. And the thing that is somewhat scary to me is that people who are writing legislation about this don't even know what this involves. This report may help to at least provide some definition, provide some framework, provide some common ground that people could use to build off.

In the cancer community, we are used to this stuff. We've been doing prospective randomized trials for years, and while that's not exactly what most people

think of as comparative effectiveness research, we are at least accustomed to the notion of comparing treatments in a rigorous way.

The real issue that comparative that I think comparative effectiveness is addressing is that if you know that something works from a well-designed prospective clinical trial, how do you then know how well it works when it's deployed out into community practice?

TCL: *So it's efficacy vs. effectiveness?*

SCHILSKY: Exactly.

TCL: *Is it possible to do an effectiveness study in oncology?*

SCHILSKY: You could do the so-called big, simple trials, where you try to construct a trial that would be as close to the way things might go in clinical practice as possible. And that might be the best you can do. The alternatives might be you could do observational or registry studies, where you just collect information about what happens to people. But you lose a lot of information there, because you don't really control what the treatment is. You don't have any way of knowing how various treatments are selected for various individuals. But there are some things that can only be tested in that way, so some information is probably better than no information.

Obviously, every doctor wants to know what is the treatment that is most likely to be beneficent for their particular patient, and if you have various treatments to choose among that seem to be similar, if you had some direct head-to-head comparisons, so you could choose on efficacy or toxicity or cost. Those are reasonable criteria to use, as long as by choosing on cost you don't sacrifice efficacy.

TCL*: How are the cooperative groups going to play this?*

SCHILSKY: I think the position from the groups is likely to be that we do this stuff. In fact, the groups—because they are publicly funded—are the only entities that are really able to directly compare treatments that the drug companies themselves may not want to directly compare. Because there is not necessarily an advantage for companies that make two very similar drugs to compare them head to head. That's something the groups can certainly do in an objective, unbiased and definitive way.

I think the big issue for the groups is going to be the tradeoff between improving clinical decision-making and advancing the science of oncology, because most of us in the groups like to think of ourselves as doing cutting-edge research that advances the science of oncology and leads to incremental improvements in current standards of care, not just defining what among the prevailing treatments is best used in certain circumstances.

Where it could get interesting, though, is if we begin to build in biospecimens and biomarkers.

Because then, instead of saying that there are three taxanes we could compare head to head in treating advanced breast cancer, we could begin to say that maybe we could figure out whether there is a particular subset of breast cancer patients who are more likely to benefit from taxane A and a different group that's more likely to benefit from taxane B. If we can do that, then we can get the best of both worlds by trying to figure out whether there are biological subsets of patients where specific treatments work best.

That's something that could be lost in the global view of comparative effectiveness research. If you just compare things that work in a broad, general, heterogeneous population, it may appear that treatment A is not much better than treatment B, but it may turn out that in the 10 or 15 percent of the population that has some specific characteristic treatment A is much better than treatment B. If you don't take the time to sort that out, you could disadvantage some patients.

TCL: *You are adding another set of terms that nobody understands—which is "personalized medicine"—on to of this. This is superimposing one ill-defined set of concepts on top of another. How do you deal with that?*

SCHILSKY: Right. We have to try to come to some common ground as to what we are talking about so we can at least talk to each other. But in my mind, the core principles that ought to be considered in the comparative effectiveness issue are—first—it has to be built off a strong evidentiary base that's derived from clinical trials. If you don't know what works in a clinical trial, how are you going to figure out whether it works in a broad community-based setting?

Second, because in oncology in particular we are moving so much toward personalized medicine, we have to apply that concept to the whole issue of comparative effectiveness, because comparative effectiveness shouldn't be one size fits all. It should be this treatment is better in this population and that treatment is better in that population, even though two treatments across a heterogeneous population may not seem to be very different from each other.

TCL: *Is there any specific project that the groups are vying for at the moment?*

SCHILSKY: No. Not that I know of. As far as I

can tell, none of the $1.1 billion that's already been set aside for comparative effectiveness is being deployed, and no one knows how to deploy it. They are all waiting for the IOM report to come out at the end of June, which is supposed to articulate the top priorities for comparative effectiveness research. Then, presumably, that will have to be translated into funding mechanisms that the groups and others can compete for.

FOCR Report Recommends Approaches To Defining CER

The following is an excerpted text of a report on comparative effectiveness research issued by Friends of Cancer Research:

A comprehensive CER program should prioritize the linking of data from public and private entities to build upon existing data collection and research capabilities. Such an initiative would allow researchers and clinicians to analyze data in ways that have never before been possible.

It will be important not to overgeneralize these results, but observations that emerge from analyzing such data could be used to design appropriate clinical trials. This approach would support the development of "personalized" or stratified medicine.

Ultimately, we need to move closer to the development of a sustainable, "learning" U.S. health care system that develops research insights as a natural byproduct of the care process and gets the right care to people when they need it and then captures the results for improvement.

Recommendation 1: A comprehensive CER program should be developed to better identify the most effective health care options.

a. An agenda for CER should be developed by the broad heath care community to address clinically important questions where clear options exist.

Policymakers planning the expansion of CER should develop a national agenda for CER on high-priority, clinically important medical questions, in conjunction with a diverse and broad range of stakeholders in health care. CER should focus primarily on generating evidence about the effectiveness of health care options and clinical outcomes that result from different medical interventions for the same condition.

Such outcomes could include survival, harm, response rates to therapy, quality of life, and/or impact on the health system (e.g., amount of required follow-up care). It is important that the agenda be coordinated across government agencies and, to the extent possible, with international officials, so that research conducted in the United States and other countries is not unnecessarily duplicated.

b. CER studies should examine the totality of health care options for a given condition.

CER could include research [on] preventive interventions, screening tests, diagnostic tests, treatments, follow-up strategies, and end-of-life care, as well as of community-based interventions (e.g., programs to encourage smoking cessation). For any particular question, however, it is unlikely that prevention, diagnosis, and treatment will all play a role.

Drug-versus-drug studies of comparative effectiveness are sometimes considered more feasible. For many conditions, a larger body of evidence is already available. It is important to bear in mind, though, that prescription drugs account for only about 10 percent of total U.S. health care spending. It is also important to consider that for many conditions, the use of a drug therapy may be only one of several options. For example, most cancer patients are rarely treated with just one drug. Instead a complete treatment regimen may include several drugs, radiation, or surgical procedures in varying sequence.

c. CER studies should examine racial, ethnic and geographic variations in care that affect health outcomes, as well as socioeconomic factors that may limit access to or affect the type of medical care provided.

There is tremendous variation in the use of a wide range of health interventions from one region of the United States to another. The differences appear to be due to discretionary decisions by physicians that are influenced by the local availability of hospital beds, specialty physicians, imaging centers and other resources—and a payment system that greatly rewards growth and higher utilization.

CER studies should generate information about different treatment approaches to disease management that may improve or negatively impact outcomes.

In some cases, the variation may stem from insufficient evidence about what is most effective. For localized prostate cancer, for example, there is significant geographic variability in medical practice.

CER studies should also consider sex, race and ethnicity (and other socioeconomic factors) in recognizing and accounting for the variation in outcomes of medical treatments. Similarly, CER studies should also examine socioeconomic factors that may affect treatment decisions. More than 45 million Americans lack health insurance, and a similar number have poor coverage or lack insurance altogether part of the year.

d. CER studies should be designed to evaluate clinical outcomes across a variety of settings and patient populations to provide usable information to patients, providers, and payers.

CER should incorporate patient-reported outcome measurements (PROs)—including quality of life data—as an additional component for evaluation. In some circumstances, treatment-related changes in PROs can influence the clinical decision-making process based on the needs and goals of the patient.

Recommendation 2: A comprehensive CER program should link data from public and private entities to build upon existing data collection efforts and research capabilities.

a. The expansion of CER activities should prioritize public-private coordination and linking of data from clinical research networks and health care databases to generate hypotheses.

A coordinated effort to link currently isolated public and private databases has the potential to generate an unprecedented amount of information for a variety of research activities. Given the variety of available data sources and differing uses of data, minimum standards of acceptable data quality will be essential to ensure validity of data collection efforts. Federal leadership and support will be needed to advance this project.

The databases routinely established, maintained, and audited for clinical research (and in some cases, preclinical research) contain detailed information about individual patients and their health outcomes. These data sets offer a potentially valuable source of information for CER. Yet clinical data sets from randomized clinical trials often include a relatively homogeneous patient population and take a long period of time to establish. Frequently, such datasets are not configured to be readily combined with other data sets, or are proprietary to manufacturers.

To begin to address the challenges to linking and sharing information from clinical databases, biospecimen repositories, and clinical researchers in the field of oncology, the NCI has developed a biomedical informatics infrastructure to enable cancer researchers, physicians, and patients to share data and knowledge. The cancer Biomedical Informatics Grid (caBIG) was established by NCI and its Cancer Centers as a pilot project in 2003 with a 3-year budget of $60 million. In 2007, caBIG advanced into an enterprise phase with the goal of connecting the entire cancer community, including NCI-designated Cancer Centers, other NCI programs, other NIH institutes and interested federal health agencies, industry y groups, and the broader biomedical research community.

By providing a unifying biomedical informatics platform, the caBIG infrastructure and tools have the potential to enable researchers and clinicians to answer questions about interventions for cancer and other conditions more rapidly and efficiently, thereby accelerating progress in research and the translation of research into clinical practice.

Several medical communities have begun developing large-scale prospective databases that allow for collection and analysis of clinical and disease biomarker data that will ultimately be used for clinical trial-matching and potentially as a clinical decision-making tool. The Total Cancer Care (TCC) Program launched by the Moffitt Cancer Center in Tampa, Florida, for example, is an innovative project that is clinically following more than 28,000 patients in 16 different communities throughout their lifetimes, storing tumor specimens from these patients for molecular analysis, and collecting patients' clinical data for use not only in treatment but also in research.

Administrative databases such as insurance claims databases, though not as detailed and not as expensive to generate as clinical databases, are another potentially valuable source of information on health outcomes and associated factors. Private insurers such as UnitedHealth Group and others routinely collect a wide array of data on individual patients' characteristics, medical care received, and the outcomes experienced for their covered populations. Such databases enable private insurers to better understand the services that they are paying for and to gain valuable information on health outcomes associated with the use of those services.

Blue Health Intelligence, developed by the Blue Cross Blue Shield Association, is beginning to bring together the claims experience of 80 million plan members nationwide. The ability to collect longitudinal data might be greatly enhanced if a system for patient identification that would be voluntary and not be used for punitive purposes could be structured to capture the large population of patients who shift to multiple different payer systems over the course of their medical history. Comparable information can be gained by examining government-operated

Medicare and Medicaid claims databases or data from the Veterans Affairs hospital systems. The move to electronic health records for all Americans may further enrich public and private insurers' databases with data from patients' EHRs, though all or most shared data will be deidentified at an early stage.

A critical element of this expanded data-network

model is an established set of policies and procedures to promote data sharing among patients, investigators, health systems, third-party payers, and others.

b. Research through an expanded data network should be used to assist systematic reviews, generate data from real-world clinical practice, and develop new methods of outcome analyses and modeling.

The information on health outcomes gained by mining and analyzing data from existing clinical and other databases must not supplant more scientifically rigorous data. Information produced through data mining represents a lower level of evidence and should be treated as such and not result in clinical decisions in the absence of corroborating evidence.

In areas where a higher level of evidence is not available, mining and analyzing data will generate information associated with the use of health interventions among real-world patients in real-world clinical practice settings and provide a foundation for designing hypotheses for further clinical research.

The oncology community is investing in several efforts that will create useful information on health outcomes that can be used to supplement data from RCTs. At a cost of more than $34 million, the NCI-funded Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) is enrolling population-based cohorts of patients newly diagnosed with lung and colorectal cancer from multiple regions and health care systems, including approximately 11,000 patients to date.

c. Although observational real-world studies have limitations, secondary analyses of existing data should be used as an initial step to identify information gaps, provide transparency to research priorities, and generate hypotheses for which further clinical trials and research may be necessary.

The FDA Sentinel Network aligns established data sets to allow probing for questions regarding adverse events experienced with the use of a drug therapy. If a safety signal is detected through this network, specific clinical trials may be required to fully establish a causal relationship between the treatment and the clinical outcome identified through secondary data analyses.

Effectiveness studies require accurate and very detailed clinical information. It will undoubtedly be more difficult to create a national data system that links large clinical and other databases for research to compare the effectiveness of health interventions, than to create a national data system to detect safety signals such as the FDA Sentinel Network. The collaboration of public and private entities will be required to create such a network, facilitate interoperability, take necessary steps to ensure privacy, and establish standards for the conduct, analytic methods, and reporting of all CER studies, including registration of studies. In the realm of CER, analyzing data from existing clinical research and other databases could be a tool that helps identify specific subpopulations that respond differently to a particular treatment or other health care intervention. As an example, data from a high-quality database could be analyzed to examine whether one of three particular interventions resulted in reduced hospitalization times.

Recommendation 3: CER studies should support the development of "personalized" or stratified medicine.

a. Emphasis should be placed not only on the "average" patient, but also on the minority who experience prolonged survival or improved quality of life and who can be identified with biomarkers or other clinical characteristics.

Approval of drugs by the FDA and formulation of the standard of care for particular types of cancer has often depended on RCTs that demonstrate prolonged survival or improved quality of life after different kinds of treatment. In conducting these trials, patients are sorted according to known characteristics that might influence outcome and then randomized to different treatment groups, making each group of patients as similar as possible. Thus, the improvement in outcome established by these trials applies to the "average" patient with cancer from a particular organ. Improvements in overall survival are generally measured at the 50th percentile and can ignore a significant minority of patients who experience a dramatic prolongation of time to progressive cancer growth or improvement in symptoms.

b. Analyses of data from an integrated data network should be per formed to identify factors that contribute to disease susceptibilities and differences in clinical outcomes.

Instances of the value of molecular subgrouping of patient populations are emerging. For example, genotyping patients for a particular gene called CYP2D6 may help indicate differences in drug metabolism rates. However, the genotyping test itself and understanding how to specifically tailor treatment decisions based on expression levels will require further study. The aggregation of large numbers of clinical outcomes as a data "input" for prospective studies, combined with the genotyping of all cancer patients, would provide the advantage of a new generation of "molecularly

informed" CER that would have the multiple benefits of learning how best to target drugs to the appropriate patient subgroups; how to avoid unnecessary adverse events; and how to optimize cost effectiveness by treating only those patients who will respond to a given therapy.

The addition of patient-reported data, including the patient-reported phenotype, patient-reported quality-of-life, and other patient-reported outcome information, will enhance the development of personalized care. Future development of a nationwide (if not global) electronic health record of all patients will facilitate such molecularly informed, patient-centered, comparative effectiveness, making it easier to execute the seamless continuum known as the "learning" health care system.

Part of the challenge to achieving personalized medicine is the chronic problem in biomedicine of institutional silos. Data sharing is often not done within one institution, and it rarely occurs between and among different institutions or biomedical sectors.

In 2008, to provide a model for collaboration among all the sectors of biomedicine—including diagnostic and therapeutic product developers, academics, payers, patients, consumers, laboratories, and others—NCI launched an initiative called the BIG Health Consortium.

This consortium conducts projects that link clinical care, clinical research and scientific discovery, using the tools, infrastructure and standards of caBIG.

To support the growth of personalized medicine in the meantime, the analysis and mining of data from integrated data networks can be used to begin to identify factors that contribute to disease susceptibilities.

c. Prospective clinical studies (including randomized trials) should be designed to further explore real-world effectiveness, characterize subpopulations for which a therapy is effective, and emphasize the collection of biospecimens to measure predictive markers.

One type of prospective clinical study that could be used to develop high-quality scientific evidence about effectiveness that would be useful in health care decision-making is a "pragmatic" (or "practical") clinical trial.

This is a clinical trial for which the hypothesis and study design are developed specifically to answer questions faced by decision-makers. A pragmatic clinical trial selects clinically relevant alternative interventions to compare; includes a large, diverse population of study participants; recruits participants from heterogeneous practice settings; and collects data on a broad range of health outcomes (although data collection is still greatly minimized compared to standard FDA-style registration trials). Analyses of data on subpopulations in pragmatic clinical trials can be used to explore the extent to which the average benefits observed within a trial differ greatly from those that might be expected for a given individual or group.

Pragmatic clinical trials are conducted in other countries, but the major funders of clinical research in the United States—the National Institutes of Health and the medical products industry—do not focus on supporting these trials, so supply of pragmatic clinical trial data is limited. Such trials can be time consuming and expensive, and their design would be aided by the hypotheses generated through database analysis as described above. The growth of practice-based research networks and electronic health records will make it increasingly feasible to conduct large research studies in community-based practice settings.

A second option that maintains the substantial benefit of generating evidence based on randomized data while substantially reducing the burden of clinical trials at the individual patient level is use of cluster randomized trials. In these trials, randomization is performed not at the individual patient level, but rather in "clusters" (which may be treating physicians, treating locations, group practices, cities, or states, for example) which are randomized to treat all patients within the cluster the same way.

Outcomes are then compared between the randomized groups at the cluster level. This approach is particularly well-suited for trials of educational or prevention initiatives that occur at a community level or for specialized interventions that require a large investment in new technology that once in place within a "cluster", usage restrictions such as demanded by individual patient randomized trials may be problematic.

The identification of prognostic and predictive biomarkers will only be possible through prospective biospecimen collection on these trials, to allow both the prospective and retrospective analyses to associate biomarker levels with clinical outcomes.

d. CER studies should have the ability to utilize all types of research methods and explore the use of more efficient research techniques.

The use of computer models to simulate the effects of health interventions is an approach that has been suggested as an alternative or supplement to clinical trials. There are many well-designed models, including

Archimedes, a full-scale simulation model of human physiology, diseases, behaviors, interventions, and health care systems.

Archimedes is intended for problems that cannot be practically studied empirically with formal trials or other evaluation designs. The NCI has a similar effort underway, known as the Cancer Intervention and Surveillance Modeling Network (CISNET) that is using biostastistical modeling to help guide clinical and policy decisions on cancer control.

Recommendation 4: Processes should be developed to ensure that information gained through CER is incorporated into clinical practice and better informs decisions made among patients, their health care providers, and payers.

a. Processes should be determined to ensure that information generated through CER studies is evaluated and reported in conjunction with current clinical guidelines to efficiently incorporate emerging scientific evidence.

For that reason, processes should be established to ensure that information generated through CER studies is evaluated and reported in conjunction with current clinical guidelines to efficiently incorporate emerging scientific evidence. It is important to ensure that guidelines are continuously updated to reflect new research; otherwise, guidelines may hinder, not foster, improved quality of care.

In addition, research is needed to identify the best way to ensure these guidelines and findings are incorporated into practice.

b. A comprehensive CER initiative should support the design of studies that provide a rational and scientific basis for reimbursement decisions and strategies of public and private health care payers.

This is an ultimate goal and the correct infrastructure needs to be in place, rigorous methodologies enforced, and systematic approaches utilized in order for CER to be routinely used in reimbursement decision-making.

Recently, however, CMS, which administers Medicare, Medicaid, and the Children's Health Insurance Program, began instituting a policy for Medicare called "coverage with evidence development" for promising drugs, biologics, devices, diagnostics, and procedures that would otherwise not meet Medicare's evidentiary standards of being "reasonable and necessary."

Under this policy, Medicare covers the cost of treatments or tests with promising but uncertain medical benefits for patients who agree to participate in either a practical clinical trial (a real-world effectiveness trial) or some kind of registry to develop evidence about the treatment. Medicare used a similar approach in designating one center for reimbursement of cardiac transplantation decades ago when that procedure was experimental and of unknown efficacy. Other major procedures have been introduced similarly.

CMS is also developing a set of pay-for-performance (P4P) initiatives to support quality improvement in the care of Medicare beneficiaries by giving financial incentives to health care providers for high quality care. In this approach, reimbursement rates vary, and are dependent on reaching certain quality measures (e.g., treatment response, treatment outcome).

c. Physicians should receive feedback on the outcomes of their choices, as well as the costs to patients and their payers.

Communicating the results of an expanded CER program will be critical to improve medical practice and decision-making. In order to demonstrate the utility of such information, data regarding the outcomes of medical decision will help physicians better measure the results of care provided.

Infrastructure and processes should be developed so that physicians receive feedback on the outcomes of their treatment choices, including patient adherence, adverse events and treatment outcomes, as well as the charges to patients and their payers. In addition, health care organizations should routinely monitor the quality of care patients receive to ensure that existing clinical practices are consistent with evidence-based guidelines. Information showing that processes of care deviate markedly from recommendations should trigger quality improvement efforts. Along these lines, research is needed that identifies the most effective strategies for promoting the dissemination and implementation of changes in clinical practice when new evidence emerges.

d. Hospital and clinical pharmacy committees should seek and utilize robust CER findings when providing information to health care providers about treatment options.

Hospital and clinical pharmacy committees should seek and utilize national CER findings, rather than institutional analyses alone, when providing information to care providers about treatment options as well as in the routine updates and development of institutional guidelines for product use.

Professional Societies:

ASCO Policy Statement Urges Elimination Of Care Disparities

Citing stark disparities in access to cancer care and survival between minorities and whites, and between people with and without health insurance, the American Society of Clinical Oncology released policy recommendations for eliminating cancer care disparities in the U.S.

ASCO's "Disparities in Cancer Care" policy statement, published online in the Journal of Clinical Oncology, recommends several strategies to reduce cancer care disparities: increasing research into cancer disparities, increasing enrollment of minorities in cancer clinical trials, encouraging greater diversity in the oncology workforce and educating the oncology workforce about cultural issues and disparities, and ensuring equal access to quality health care.

"Decades of investment in cancer research have led to important advances in screening and treatment, and vastly improved cancer survival rates," said ASCO President Richard Schilsky. "Yet, there is a profound divide in our nation between those with access to the fruits of this research, and those without. If we are to drive down cancer death rates, this gap must be closed."

A new study also published in JCO points to the urgent need to better address the needs of minority patients in the U.S. The researchers project an increase of 99% in cancer incidence among minorities by 2030, compared to 31% among whites.

Studies show that uninsured Americans are less likely to get cancer screenings, more likely to be diagnosed with advanced stages of cancer, and less likely to survive than individuals with insurance. One in five African-Americans is uninsured, as is one in three Latinos. Studies also show that minority cancer patients, independent of insurance status, experience significantly worse outcomes than their white counterparts.

ASCO's policy statement makes several broad recommendations to increase access to health care and improve the care of minority patients.

"Only through a combination of efforts—addressing financing and delivery of care, enhancing the number and training of oncologists caring for diverse populations, and strengthening research on health disparities—can we deliver the significant achievements that are critical to improving care for all," said Otis Brawley, co-chair of ASCO's Health Disparities Advisory Group and chief medical officer for the American Cancer Society.

ASCO's policy statement calls for:

—Increasing research on the quality of care provided to minority populations and the factors contributing to poorer-quality care.

—Increasing minority enrollment in clinical trials to answer critical questions about cancer progression and treatment in minority populations.

—Increasing the diversity of the oncology workforce to provide more culturally appropriate care to minority patients, and increasing the number of oncologists who practice in underserved areas.

—Developing policies to guarantee equal access to quality health care, with a special emphasis on increasing insurance coverage and reducing economic barriers to cancer care.

"Lack of insurance is one of the biggest barriers to improving cancer care and survival in the United States," said Derek Raghavan, co-chair of ASCO's Health Disparities Advisory Group and chairman and director of the Cleveland Clinic Taussig Cancer Center in Ohio. "To eliminate disparities, it is essential to ensure that everyone has access to the most effective treatment, and to screening services that allow us to detect cancers early and prevent recurrence."

Cancer incidence among minorities will nearly double in the coming decades, according to an article published in the Journal of Clinical Oncology. The study, "Future of Cancer Incidence in the United States: Burdens upon an Aging, Changing Nation," underscores the urgency of expanding access to health insurance and improving cancer care for minority patients. The study was conducted by researchers at Lackland Air Force Base and the University of Texas M.D. Anderson Cancer Center and City of Hope Cancer Center in California.

The study projects that the total number of people diagnosed with cancer each year in the U.S. will increase 45%, from about 1.6 million cases per year in 2010 to 2.3 million cases per year by 2030. Much of this can be attributed to projected increases in the number of minorities and older adults in the U.S.

By 2030, the study estimates a 99% rise in cancer incidence for minorities – from 0.33 million to 0.66 million cases annually. In contrast, a 31% increase in cancer incidence is anticipated for non-Hispanic whites.

"As the make-up of the United States changes over the next 20 years, physician practices will have to adapt," said Benjamin Smith, lead author of the study and chief of radiation oncology at Wilford Hall Medical Center at Lackland Air Force Base. "Physicians need

to seek out training to enhance their ability to deliver care for minorities and learn how to recognize race- and age-specific differences in cancer progression and cancer treatment."

ASCO announced the first recipients of ASCO's Diversity in Oncology Initiative, funded by Susan G. Komen for the Cure. This is the first program of its kind designed to diversify the oncologist workforce and increase the number of oncologists practicing in medically underserved areas. Currently, 2% of U.S. oncologists are African American and 3% are Latino, compared with 12% and 15% of the U.S. population.

The grants were awarded in three categories:

—The Loan Repayment Program Award: Three grants of up to $50,000 each for young oncologists who have committed to providing cancer care in a medically underserved region of the United States for at least two years.

—The Medical Student Rotation Award: Four grants of $8,500 each for medical students from populations under-represented in medicine who enter the oncology field. The program allows medical students to participate in 8- to 10-week rotations in oncology. Students are being matched with a mentor oncologist, who will provide ongoing academic and career guidance through the rotation and beyond.

—The Resident Travel Award: Thirteen grants of $1,500 each for medical residents from populations under-represented in medicine to attend ASCO's Annual Meeting (May 29 to June 2 in Orlando, Florida) and be paired with a mentor onsite.

Funding for the Diversity in Oncology Initiative will continue in 2010, with additional grant dollars available to fund more students and doctors in each award category.

HHS News:

Margaret Hamburg Confirmed As FDA Commissioner

MARGARET "PEGGY" HAMBURG was confirmed as FDA commissioner by the Senate.

"Dr. Hamburg is an inspiring public health leader with broad experience in infectious disease, bioterrorism, and health policy," said Health and Human Services Secretary **Kathleen Sebelius**. "Her expertise and judgment will serve FDA well."

Hamburg served as the Nuclear Threat Initiative's founding vice president for the Biological Program. Before joining NTI, she was the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. Prior to this, she served for six years as Commissioner of Health for the City of New York and as the Assistant Director of the National Institute of Allergy and Infectious Diseases at NIH.

BILL CORR was confirmed by the Senate as deputy secretary for HHS. Corr most recently served as Executive Director of the Campaign for Tobacco-Free Kids. Previously, Corr served for 12 years as counsel to the House Subcommittee on Health and the Environment. He served as chief of staff for HHS. Corr is a graduate of the University of Virginia and the Vanderbilt University School of Law.

"Bill Corr's policy expertise and management experience will be invaluable as we work together to manage the Department and pass and implement comprehensive health reform," said Sebelius. "Bill knows our Department inside and out, and I look forward to partnering with him in the years ahead."

YVETTE ROUBIDEAUX was confirmed by the Senate as director of the Indian Health Service. Roubideaux served most recently as an assistant professor in the Department of Family & Community Medicine at University of Arizona College of Medicine. She has conducted extensive research on American Indian health issues, with a focus on diabetes in American Indians/Alaska Natives and Indian health policy. Roubideaux previously worked in the Indian Health Service as a medical officer and clinical director on the San Carlos Indian Reservation and in the Gila River Indian Community. Roubideaux is a member of the Rosebud Sioux tribe. She received her MD from Harvard Medical School and her MPH from the Harvard School of Public Health.

"Dr. Roubideaux has spent her life working to improve health care for Native Americans," said Sebelius. "She has seen the Indian Health Service through the eyes of a patient and a doctor, and I know she is the leader we need to strengthen IHS and ensure we keep our promise to provide quality health care to Native Americans."

"HARD TIMES in the Heartland: Health Care in Rural America," a new report from HHS, outlines the health care challenges facing rural communities. The report was developed by HHS staff and is available at www.HealthReform.gov.

The report indicates that nearly 50 million people in rural America face challenges accessing health care. Not only do these Americans face higher rates of poverty, they report more health problems, are more likely to be uninsured, and have less access to a primary health care providers than do Americans living in urban areas.

In the Cancer Centers:

Hyman Muss Joins UNC's Lineberger Cancer Center

(Continued from page 1)

increased the chance for breast conservation among women with breast cancer. Of the 700 NSABP member institutions in North America, Massey Cancer Center is one of the top 10 members in terms of enrollment of patients in studies. Bear's research team has been cited for providing excellent follow-up and reporting for all patients who have enrolled in NSABP studies. The Massey Cancer Center is affiliated with NSABP through its Minority-Based Community Clinical Oncology Program grant. Bear became a research investigator with NSABP in 1984. He served as study chair for two major NSABP-sponsored clinical studies, B-27 and B40, and has been part of working groups for several other studies. He also served on NSABP's Board of Directors since 1991, and served on several other committees that develop protocols for trials. . . . **HYMAN MUSS** joined the Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill School of Medicine. Muss will be a professor of medicine and will develop and lead a new program in geriatric oncology. Muss served as associate director of clinical research and division director of hematology/oncology at University of Vermont Cancer Center. He was previously at Wake Forest University Comprehensive Cancer, where he was a professor of medicine and associate director for clinical research. **Shelley Earp**, director of UNC Lineberger Comprehensive Cancer Center, said, "Simply put, Hy Muss is a national treasure. His clinical research accomplishments are outstanding, but are frankly secondary to his skills as a doctor, teacher, and colleague. We are thrilled that the University Cancer Research Fund has allowed us to bring Hy back to North Carolina to start the new, much needed Geriatric Oncology effort." Muss serves on the Board of Directors for the American Society of Clinical Oncology Foundation and for the Cancer and Leukemia Group B, and on the editorial boards of several publications. . . . **HOWARD SANDLER**, chair of radiation oncology at Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute, was named the inaugural Ronald H. Bloom Family Chair Holder in Cancer Therapeutics. The endowed chair will support research into new treatments for cancer. . . . **CENTER FOR PRACTICAL BIOETHICS** established the Kathleen M. Foley Chair for Pain and Palliative Care at its 25th anniversary gala in Kansas City. The chair is named after **Kathleen Foley**, attending neuro-oncologist in the Pain & Palliative Care Service at Memorial Sloan-Kettering Cancer Center. The center seeks to create a dialogue between medical professionals, policymakers and patients to identify and confront complicated ethical dilemmas; a key focus of these efforts is achieving balanced, practical pain care. "I'm honored to have an endowed chair established in my name at the Center for Practical Bioethics—an organization that shares my commitment to improving access to pain care and enhancing pain policy in the United States," said Foley. "With this endowed chair, the Center has elevated its level of dedication still higher to relieve pain and suffering at all stages of life." The center is identifying potential candidates for the Foley Chair, which will be funded by a $3 million endowment. Purdue Pharma has provided a lead gift of $1.5 million, and efforts are under way to raise the balance of the endowment. . . . **UNIVERSITY OF ARKANSAS** for Medical Sciences named **Kent McKelvey** the inaugural recipient of the Winthrop P. Rockefeller Chair in Clinical Genetics. The chair and genetics clinic was established with a donation from Lisenne Rockefeller, wife of the late Arkansas Lt. Gov. Winthrop P. Rockefeller. McKelvey is director of Cancer Genetics Services at the UAMS Winthrop P. Rockefeller Cancer Institute.

Funding Opportunities:

Community Clinical Oncology Program (U10) (RFA-CA-09-022) http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-022.html

Notice of Intent to Publish a Request for Applications for Research on the Biology of Estrogen Receptor Negative Breast Cancer in Various Racial & Ethnic Groups http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-024.html

NCI Announces Opportunity for Interested Investigators to Propose Candidate Biomarkers of Mesothelioma for Validation in a Unique Human Cohort and to Participate in a Working Group Meeting http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-025.html

Administrative Supplements to Promote Research Collaborations in AIDS-Associated Malignancies for Projects Currently Funded by the National Cancer Institute http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-026.html

NCI-Supported R25 Cancer Education Grant Programs In Integrative Science http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-027.html

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