

*Feinstein Kean
Healthcare, Personalized
Medicine Coalition,
and American
Association for Cancer
Research*

Turning the Tide Against Cancer

A discussion paper that interviewed some of the top experts in oncology identifies some of the cutting edge models for research, development and delivery as well as paths forward in addressing some of the major challenges.

*The Personalized Medicine Coalition, the American Association for Cancer Research, and Feinstein Kean Healthcare took a unique approach to addressing some of the major policy issues facing cancer care. The three groups organized a national conference that took place on June 12, 2012 in Washington, DC. In conjunction with the conference, they released a major discussion paper titled: *Sustaining Progress Against Cancer in an Era of Cost Containment*.*

Thirty five experts from multiple disciplines in the oncology ecosystem were interviewed for the paper. The full paper produced and edited by Feinstein Kean Healthcare and edited by Marcia Kean and Tracy Lessor can be found at www.TurningTheTideAgainstCancer.org.

The aims of the paper and the conference are to address:

- **A changing cancer care ecosystem:** Emerging evidence-generation tools and the development of new models and systems that are founded on recent scientific advances, the changing role of the patient in research, and how the cancer community is adapting.
- **Valuing innovation and progress:** Defining and demonstrating value in cancer care, stakeholder perception of value, and current approaches to measuring value.
- **Potential paths forward:** Defining actionable policy solutions to ensure continued innovation in oncology.

We have excerpted some of the findings and recommendations from the discussion paper. The excerpts have been edited for readability.

Emerging Innovative Models and Systems

Many emerging innovative models and systems show great promise for turning the tide against cancer. Although not exhaustive, the models described below are among those most commonly mentioned by interviewees.

I-SPY2: Adaptive Clinical Trials

With its focus on real-time evidence generation and implementation, the creative I-SPY2 adaptive clinical trial was identified in interviews as a noteworthy addition to conventional randomized, controlled clinical trials. This trial design serves as a model not only for future oncology trials, but for a Rapid Learning Healthcare System overall, in several ways:

- Utilizes outcome data from each patient as she progresses through the study to inform treatment assignments for the next patient;
- Incorporates pre-competitive collaboration for biomarker identification;
- Streamlines the trial model, resulting in reduced length, fewer patients, and fewer requisite resources;
- Tests investigational agents from multiple

companies in combination with standard of care treatments;

- Tests investigational agents in newly diagnosed patients—a potentially curable patient population;
- Utilizes a unique public-private partnership and collaboration model among the Foundation for the National Institutes of Health (FNIH), the Food and Drug Administration (FDA), the National Cancer Institute (NCI), more than 20 leading academic cancer centers, the Safeway Foundation, QuantumLeap Healthcare Collaborative, and patient advocates, and receives funding from a number of pharmaceutical companies; and
- Makes study data publicly available.

Moffitt Total Cancer Care

By collecting clinical data throughout a patient's lifetime, molecularly profiling all tumors, and making data accessible for patients, clinicians, and researchers, the Moffitt Cancer Center's Total Cancer Care™ project is one example of a comprehensive strategy for improving patient care through a rapid learning model. This approach, which has enrolled more than 80,000 patients in its observational study:

- Leverages partnerships with patients, community clinicians, industry, and academia to focus on new technologies to improve screening methods, define new standards of care, and develop new therapeutic technologies;
- Collects and stores a large number of patient biospecimens, genomic profiles, and clinical information for future in-depth analysis by researchers to improve the standard of care and drive discovery;
- Provides standardized data quality and easy access to information through a hub-and-spoke model;
- Follows patients throughout their lifetime, and provides individualized, evidence-based decisions for screening, diagnosis, and treatment of cancer based on integration and analysis of

data from scientific discovery and health outcomes; and

- Incorporates preventive measures, including the study of genetic predispositions, impact of lifestyles, and integrative medicine.

Multiple Myeloma Research Foundation

By leading multiple dynamic, innovative research activities, the Multiple Myeloma Research Foundation has created a unique patient-centric and patient-driven model that:

- Drives collaboration among patients, academic and community medical centers, industry, and payers;
- Encompasses a tissue bank, clinical network, and a genomics initiative;
- Incorporates pre-competitive collaboration: consortium members have priority access to data for six months before it is shared on a public portal, which is being designed to be similar to an Amazon system; and
- Is building an online community for myeloma patients and directing them to trials and new treatments that might be appropriate for them.

This model is being widely credited for significantly increasing the number of therapeutic options available to multiple myeloma patients, as well as increasing the expected survival time for patients.

Army of Women/ Dr. Susan Love Research Foundation

The Army of Women initiative was cited as an important model for mobilizing consumers and researchers to focus on prevention efforts and is one example of the broader emergence of patient engagement models. This initiative:

- Empowers the consumer to control the research agenda and the data;
- Deploys a consumer-owned, consumer-driven participatory model; and
- Recruits healthy women to partner with researchers on prevention studies.

NCI's Biospecimen Research Network /cancer HUMAN Biobank (caHUB)

The National Cancer Institute's Biospecimen Research Network and caHUB (which develops evidence-based best practices for the collection, process, storage, and analysis of biospecimens) is a key entity for the development of biospecimen standards. This program:

1. Supports scientific research to bolster the evidence base for biospecimen collection, handling, and processing practices;
2. Leads the development of policies and processes for collection and management of biospecimen resources; and
3. Partners nationally and internationally to harmonize biospecimen and biobanking standards.

Measuring Value and Aligning with the State of Science

The interviews revealed something of a paradox: there is an exponential increase in the amount of information available to guide patient care decisions, yet there is also broad consensus that current approaches to assessing the value of innovative technologies and care delivery, (e.g., comparative effectiveness research (CER), cost-effectiveness analysis (CEA), and health technology assessments (HTA)), are far from optimal in this new era of rapidly advancing personalized oncology. Some interviewees view this as a tension between a "dynamic" cancer ecosystem marked by rapid advances in technology, scientific research, and clinical evidence on the one hand, and "static" tools for value assessment on the other. Many call for significant reforms, or entirely new models, for generating and assessing evidence of value in oncology.

The rapid acceleration of science and technology that is taking place within oncology will require an acceleration of the evidence generation capabilities around value. Equally important, new evidence assessment capabilities are

needed in order to provide accurate, patient-centered, and current assessments of clinical and economic value. Current CER, CEA, and HTA models will become increasingly challenged by personalized medicine because point-in-time assessments of treatments will become obsolete as patients are continually monitored and reassessed to identify optimal treatment regimens designed for their precise molecular subtype to include targeted therapies, personalized treatment cocktails, and biomarker-driven clinical decision-making.

The biggest limitations identified in current value assessment approaches are that they are unable to recognize and support the incremental nature of the evolution of value; are not dynamic, continuous processes and thus cannot keep pace with advancements in science and medicine; and give inadequate consideration to patient quality of life, patient preference, and indirect measures of value like productivity. These challenges and limitations led some interviewees to suggest that the United States consider a new system that provides alternative approaches to measuring and applying value-based information. As these measurements will likely add more cost into the system, they said, it is important to invest in the *right* measurements and assessment models. This perspective is consistent with recent literature highlighting the challenges with health technology assessments in oncology and a recommendation for an increased focus on patient-provider decision-making versus centralized decision-making as the locus of evidence-based value judgments.

The call for a new system is not inconsistent with calls for more evidence to inform oncology decision-making, yet it does suggest that simply putting more money and emphasis on existing value assessment models will not lead to success. There was broad recognition that new approaches are needed

in which CER, CEA, and HTA models better align with progress in cancer care by:

- **Recognizing divergent perspectives on value and centering on patient value as defined by patient needs and preferences.** Numerous interviewees acknowledged the challenges of making value more patient-centered: there are a variety of dimensions that constitute value, including overall survival, quality of life, and impact on the caregiver; patient preferences can change depending on where a patient is in the disease process; and patients may place greater emphasis on certain outcomes than other stakeholders (e.g., quality of life improvements).
- **Personalizing value measurements.** Interviewees highlighted the limitations of current models of CER and CEA that measure population averages and thus do not take into consideration biological differences among patients and their tumors, which is the foundation of personalized medicine. This limitation suggests that more sophisticated approaches are needed that can handle the extreme heterogeneity of cancer and consider value at the individual level instead of at the population level.
- **Incorporating broader measures of value.** Many interviewees suggest that broader measures of value such as patient preference and quality of life should be incorporated into value assessments. Some interviewees note that some metrics, such as quality-adjusted life years, can incorporate these broader measures. Others, however, note that such measures often do not reflect variations in patient values and may be better-suited for societal versus individual value judgments. This may indicate a disconnect between methods for assessing broad societal value at the policy level, and tools designed to support value-based decisions at the

level of individual patient and physician treatment decisions.

- **Measuring evolving value of innovative treatments.** It is generally true in medicine that patient outcomes improve over time as we gain experience with new treatments and interventions. For example, patients who receive a transplant live significantly longer today than they did when these procedures were first introduced because we have developed a greater understanding about who should receive them, and the technologies of that approach have improved. Another example is the benefit of Velcade® (bortezomib) in increasing the overall survival of patients with newly diagnosed multiple myeloma by 13 months—knowledge that only became apparent five years after the drug's FDA approval. In addition, some interviewees pointed out that progress frequently occurs through an incremental process in which individual advances ultimately yield significant gains for patients. One example of this is colorectal cancer, where patients now benefit from earlier intervention with multiple treatment options. For this reason, interviewees opined that value assessment must be a dynamic, continuous, prospective process because the true value of a treatment to patients and society—its clinical *effectiveness*—cannot be known at the time of FDA approval.

Potential Paths Forward

Interviewees underscored some of the most important innovative scientific discoveries that are creating new possibilities for turning the tide against cancer, in addition to heretofore unimagined challenges, such as cancer's extreme heterogeneity and adaptability, particularly in later stages of disease. These discoveries have brought us to a true turning point—one in which opportunities can be realized and barriers

Does your complaint management system
provide value to your company?

HOW MUCH DO YOU KNOW ABOUT QSR & ISO 13485 Regulations?

The “Medical Device Complaint Handling”
Special Report provides a comprehensive view
into the complaint management process taking you
step-by-step through the regulatory hurdles and
frequently overlooked fine print. This report was
developed by experienced experts and will answer
many questions including: what should I do first
when I receive a complaint, how can I prevent the
most common complaint failures, and how can I
successfully integrate my complaint handling
system fully into my CAPA program?



Visit:

<http://www.elsevierbi.com/mkt/webinars/SR/ACSR0611LP.html>

BONUS

**We've also included an exclusive detailed checklist
for selected US regulations.**

For more information contact EBI Customer Care at:
(800) 332-2181 or (908) 547-2159 or email us at custcare@elsevier.com

overcome—during a time of unprecedented pressure on federal spending for research, as well as concerns that cost containment measures are becoming more likely.

This section organizes the major ideas presented by interviewees as potential solutions, which collectively could begin to define a path forward to sustain innovation and turn the tide against cancer. In addition to identifying many important opportunities, barriers, and potential paths forward, participants consistently stress the need for a sustained, community-wide commitment to solutions. The approaches described below are intended to spur discussion of a framework that could form the basis of that commitment.

Support the Shift to Patient-Centered Care in Oncology

A consistent theme among interviews was the need to define value from a patient-centric perspective, which requires bringing the patient into the value equation in more meaningful ways. Interviewees put forth the following suggestions:

- Engage patients in defining value and value-based research.
- Define and utilize value measures that matter to patients (e.g., quality of life and patient preference).
- Engage patients and caregivers in treatment decision-making.
- Support physicians, patients, and caregivers in shared decision-making (evidence-based value decisions at the individual level) through the use of clinical decision support tools.

Develop Regulatory and Reimbursement Policies to Advance Personalized Medicine

A consistent theme among interviews was that innovation can drive value, and personalized medicine is a key element of innovation for oncology. Specific suggestions to sustain innovation and advance personalized medicine include:

- Develop clear yet flexible regulatory pathways that can evolve to keep pace with advancements in science and medicine. Many interviewees believe new pathways and standards must be defined to support the rapid, efficient development of new targeted oncology therapies and diagnostic tests.
- Improve coverage and reimbursement policies to support adoption of medically appropriate personalized medicine products. Ensure evidence standards are appropriate for novel interventions such as new molecular diagnostics.
- Structure new payment models, including accountable care organizations and cancer care pathways, in ways that enable physicians to tailor care based on genetic or other diagnostic information, clinical circumstances, or patient preferences. This will allow for appropriate adoption of advances in care that may have higher initial costs but yield higher value over time.

Advance Research on Molecular-Based Biomarkers

Most interviewees agree that a lack of standards-based, high-quality, clinically annotated biospecimens and a lack of standards-based technologies and methodologies used to interrogate these biospecimens are significant barriers to biomarker discovery and development. These issues help explain why the majority of biomarker candidates discovered cannot be clinically validated and why many biomarker studies cannot be replicated.

Clear standards, widely accepted methods, and more flexible policies governing the use of biospecimens are needed to encourage the development of more biomarker-based tests needed to move personalized cancer care forward. Improper methods of biospecimen collection, storage and/or handling can change the biology of the specimen, meaning that the bio-

specimen does not reflect the molecular characterization of the patient's tumor, and data obtained from such biospecimens can be misleading or unusable. Researchers are also challenged by the lack of clinical annotation and by legal, ethical, and policy restrictions that govern biospecimen use. Furthermore, researchers use various technologies to discover biomarkers and each of these technologies lack standard methods and reagents, which results in pervasive problems with reproducibility and hinders the development of biomarker-based tests.

A common theme among interviewees was the need for quality and reference standards for biomarker discovery and validation research. Without these standards, valuable tissue samples will be wasted and biomarker discovery and clinical validation will be compromised. Specific suggestions include:

- Incentivize the development and adoption of standards for biospecimen collection (including clinical annotation), handling, storage, and analysis.
- Support a national (or international) biorepository that is managed either by government or by a neutral collaboration among organizations to serve as 'honest broker'.
- Incentivize the development and use of standards for '-omics' technologies used in biomarker discovery.

Support the Development of Molecular Diagnostics

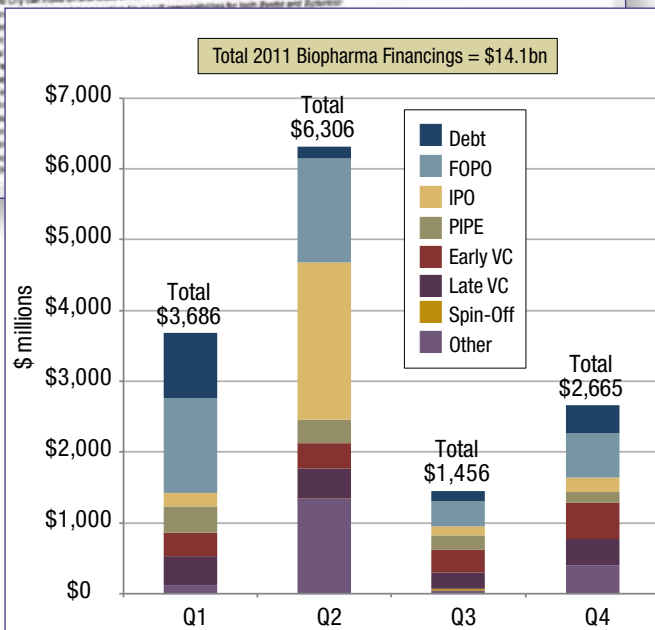
Given the current regulatory and reimbursement environment for diagnostics, many interviewees believe that the business model for the development of molecular diagnostics is challenged. A disconnect exists between the regulatory pathways for drugs and diagnostics. The lack of regulatory clarity for diagnostics creates great uncertainty and risk, which in turn undermines and discourages innovation.

STRATEGIC TRANSACTIONS



Strategic Transactions, your most trusted and reliable source for analyzing and tracking health care deal activity, has joined ElsevierBI.com with a fresh new look and improved functionality!

- Added search capabilities
- Ability to share, save and print deals
- Ability to search across all publications, company profiles AND deals data
- Direct links to deal-related analysis from Elsevier Business Intelligence sources including "The Pink Sheet" and IN VIVO
- Daily deal updates
- Enhanced compatibility with mobile devices
- Simple sign-up for any of our free E-Letters, Blogs and Publication Newsletters
- ...and more!



Learn more about the many benefits and new features at
<http://www.elsevierbi.com/STEBI3>

See what you've been missing! Request a free, personal demonstration today.
<http://www.elsevierbi.com/STDEMO>

The time, resources, and skill sets required to develop innovative molecular diagnostics are not compatible with a payment policy that largely considers time and materials in the reimbursement calculation. As a result, randomized, controlled clinical trials are prohibitively expensive for molecular diagnostic innovators and such trials may not be justifiable based on the expected return on investment. Overall, interviewees stressed that the desired state of personalized cancer medicine will not be possible without a flourishing pipeline of molecular diagnostic tests. Specific suggestions to support their development include:

- Develop regulatory and reimbursement policies that incentivize the development of innovative diagnostic technologies needed to diagnose disease and predict cancer risk.
- Foster a regulatory and reimbursement environment that values and rewards the co-development of innovative targeted treatments and companion diagnostics and incentivizes their co-development through tax incentives or other funding mechanisms.
- Support provisional approval and coverage for molecular diagnostics.

Align CER and HTA with the Patient and the Science

There is broad support among interviewees for utilizing CER and HTA in helping to assess the value of innovative technologies; however, there is also broad agreement that these tools must adapt to the emerging science. Specifically, CER and HTA must align with patient needs and values, as well as the emerging science and changing clinical practice of oncology, and they both must shift from a retrospective, static paradigm to a prospective, dynamic paradigm. Absent this shift, these tools will lag further and further behind the rapid pace of change within oncology science and clinical practice.

Several interviewees suggested that this shift may require the creation of a Rapid Learning Healthcare System in oncology described below. In addition, suggestions include:

- Develop new tools and approaches to CER and HTA that reflect a commitment to patient engagement and adopt policies that match this commitment.
- Engage physicians, clinical experts, and scientists with relevant subject matter and technical expertise to guide CER and HTA. The oncology community has strong mechanisms for defining and disseminating knowledge via societies and clinical experts, but these mechanisms (e.g., professional society guidelines) are frequently disconnected from policy-level decision-making. Steps should be identified to more directly link these capabilities in the clinical community to payers and policy-level decisions. For example, the Patient-Centered Outcomes Research Institute (PCORI) should establish advisory panels of clinical experts and scientists from the fields of oncology and personalized medicine to inform their agendas.
- Recognize and accommodate biological differences among individual patients and patient sub-groups in CER and HTA. Some interviewees noted that, done well, CER and HTA can help optimize decision-making by patients and physicians because these tools may ultimately provide more information about differences in patient sub-groups. Many interviewees also cautioned, however, that CER and HTA frequently are performed and applied in ways that obscure the differences and render results based on broad population averages. Consensus should be developed on approaches to CER and HTA that are more patient-centered by better reflecting individual and sub-group differences.
- Establish the methods and infrastructure (e.g., linked observational data

sets) to guide patient-centered research on real-world effectiveness.

- Develop tools that effectively disseminate meaningful information to patients and providers.
- Incorporate into HTA a wider range of value measures, particularly those that matter to patients but often are overlooked, such as quality of life or patient experience.
- Develop flexible policies for CER and HTA that allow for continued learning about new tests, treatments, and interventions.

RPM

Comments? E-mail the editor at ramsey.baghdadi@previsionpolicy.com