

Where ASCO's New Cancer Care Value Plan Falls Short

BY LOLA BUTCHER

The proposal for a “value framework” that could be used to evaluate cancer treatment options is a great idea, but putting a framework down on paper shows just how difficult it is to consider value in oncology.

That’s the consensus of observers who shared their perspectives on the framework proposal put forth by the American Society of Clinical Oncology (*JCO* 2015;33:2563-2577).

“There’s no question that every specialty should be looking at value—and oncology, in particular,” said Thomas Feeley, MD, Head of the Institute for Cancer Care Innovation at the University of Texas MD Anderson Cancer Center. “This is very timely, and I think they have a tremendous approach to looking at value for medical oncology.”

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Myeloma Exome Analysis Uncovers Clinical Insights

BY KURT SAMSON

A study using whole exome sequencing in approximately 500 myeloma patients has revealed a range of different mutation types in genes and molecular pathways—some negative and some neutral—that appear to influence patient survival (*Blood*, doi.org/10.1182/blood-2015-05-644039).

Using the findings, the researchers also used the data to develop a staging system to better identify patients at higher risk of relapse and premature death. The study was funded by the United Kingdom’s Institute of Cancer Research at Royal Marsden Hospital’s Division of Molecular Pathology, as well as the Fondation Française pour la Recherche contre le Myélome et les Gammopathies, in Paris.

Believed to be the first whole exome analysis exclusively among myeloma patients, the results are published online ahead of print in the *Journal of Clinical Oncology* (doi: 10.1200/JCO.2014.59.1503). The team also used the data to develop a staging system to better identify patients at higher risk of relapse and premature death.

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Conference Sounds Alarm about the Dangers of Overdiagnosis

BY PEGGY EASTMAN

BETHESDA, MD—Some 350 participants from throughout the world and from a broad range of professional backgrounds gathered here on the grounds of the National Institutes of Health for a conference focused on pre-

venting overdiagnosis and overtreatment in medicine, exploring the concept that more isn’t always better when it comes to high-quality care.

This third annual meeting, which had the theme “Winding Back the

Harms of Too Much Medicine,” was co-sponsored by the National Cancer Institute’s Division of Cancer

Prevention and the University of Oxford’s Centre for Evidence-Based Medicine. Conference partners included the Dartmouth Institute; Bond University’s Centre for Research in Evidence-Based Practice; *BMJ*; and *Consumer Reports*.

The conference was designed to examine the factors driving overtreatment for nonprogressive disease—overtreatment that could cause harm, said Barry Kramer, MD, MPH, Director of NCI’s Division of Cancer Prevention.

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CONFERENCE SOUNDS ALARM ABOUT THE DANGERS OF OVERDIAGNOSIS

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Cancer was a major focus of the meeting, but other conditions—such as attention deficit hyperactivity disorder, concussions in sports, female sexual function, and cardiac illnesses—were also included.

“This is really a ‘newish’ campaign,” said *BMJ* Editor Fiona Godlee, MD, in introducing the concept of overdiagnosis at the meeting. But, she noted, the issue is now becoming embedded in people’s consciousness, and health professionals need to be skeptical about their own perceptions and biases in providing care.

For patients, overdiagnosis can cause emotional and psychological distress, financial strain, medical expenses, work interruption, the inconvenience of getting to medical appointments, and physical harm.”

‘Incredibly Emotional’

“This is a subject that is incredibly emotional for some people,” said keynote speaker Otis Brawley, MD, MACP, the American Cancer Society’s Chief Medical and Scientific Officer and Executive Vice President for Research.

He defined overdiagnosis as the diagnosis of “disease” that would not cause symptoms or death during a patient’s lifetime. Overdiagnosis, he said, “is a side effect of efforts to screen and detect disease early. ‘Overdiagnosis exists in a number of diseases, but is an especially important issue in cancer medicine.’”

That, he said, is because the prevailing common mantra of cancer treatment has been “all cancers are bad,” and “the best way to deal with cancer is to find it early and cut it out.”

But today, Brawley continued, a new “21st century definition of cancer” is needed, based on the molecular fingerprint of the cancer, not just its pathology. “Despite our tremendous advances in technology, we still use a mid-19th century definition. We need a definition of cancer that will incorporate both histology and genomics and appreciate the varying biologic behaviors of tissues that fulfill the profile of malignancy.”

A new mindset is necessary, said Brawley, one that goes beyond pathologic profiling to instead ask about small lesions: “Do these look like something that is genetically or genomically programmed to grow, spread, and kill?” As an example of when that question is needed, he cited small prostate-specific antigen (PSA)-detected prostate cancers.

Overcoming the Fear Factor

If small lesions will not grow, spread, and kill, the diagnosing and treating small lesions constitutes unnecessary treatment, he said. But, the fear factor needs to be overcome to reduce overdiagnosis. In oncology, “we’ve been using fear as a tactic for a long time; I think it’s a good thing that we’re challenging it,” Brawley said.

Asked if he thinks oncology is moving in the direction of a new biologically based definition of cancer likely to reduce overdiagnosis, he said yes, citing panels of biomarkers for the molecular classification of tumors such as breast cancer. But, he noted, progress is slow, in part because biomarkers need to be validated, which is an expensive process.

Kramer also noted that he thinks more precise, biologically based classification of cancerous tumors is on the rise, a trend that should cut down on overdiagnosis and unnecessary treat-

Buck Breast Care Center, Professor in the Departments of Surgery and Radiology, and Affiliate Faculty in the Institute for Health Policy Studies at the University of California, San Francisco. She said that more early-stage, molecularly low-risk tumors are now being diagnosed, but also cautioned that tumors with aggressive biology are being identified as well.

“Our approach to early detection has to evolve as our understanding of breast cancer biology evolves,” she said. “We need to develop better tools to identify indolent tumors at the time of diagnosis, refine our targets for screening, and our thresholds for biopsy.”

Unprecedented Opportunity...

“Screening has generated a great deal of controversy, and there is no consensus on guidelines. We should initiate modern trials of screening that help us to continue to improve our approach to screening. We have an unprecedented opportunity to advance the field if we incorporate our current understanding of breast cancer biology, advances in risk assessment, and imaging technology to learn who is at risk for what kind of cancer and adjust accordingly.”

Esserman cited the new WISDOM (Women Informed to Screen Depending on Measure of Risk) trial, announced in March and funded by the Patient Centered Outcomes Research Institute (PCORI) as an example of a personalized (risk-based) versus annual

screening approach. The goal is to learn if the personalized approach is as safe as annual screening, is preferred by women, is less morbid, and facilitates the adoption of prevention. If so, the new approach could reduce overdiagnosis.

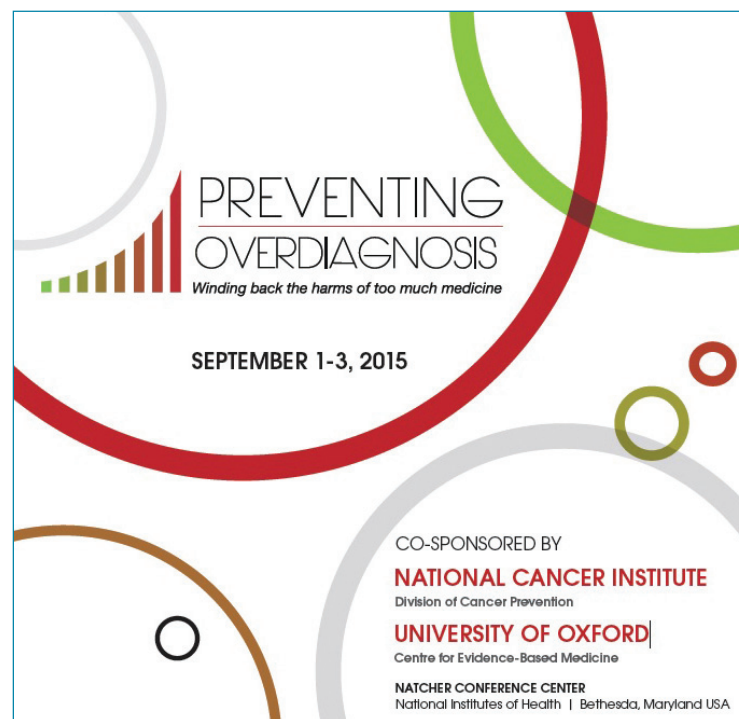
Reducing Overdiagnosis in Children

Because children have their whole lives ahead of them, reducing overdiagnosis in pediatrics is especially important, said another keynote speaker, Virginia A. Moyer, MD, MPH, Vice President for Maintenance of Certification and Quality for the American Board of Pediatrics.

For example, she noted that radiation therapy in childhood can increase a child’s lifetime cancer risk. One example of identifying and reducing overdiagnosis in pediatrics

“We need a 21st century definition of cancer that incorporates both histology and genomics and takes into account varying biologic behaviors.”

—Otis Brawley, MD, MACP



ment. “We’re heading in the right direction... I think this is an important way forward.” He said that NCI considers the funding of biomarkers to define the biology of cancers more specifically to be a high research priority.

For example, the newly launched multicenter NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) trial, which opened for enrollment in August 2015, plans to obtain tumor biopsy specimens from as many as 3,000 patients initially (*OT 8/25 issue*). Advanced DNA sequencing will be used to identify tumors with genetic abnormalities that may respond to molecularly targeted drugs chosen for the trial.

In breast cancer, molecular tools are already enabling a more precise classification of tumor types, said another of the keynote speakers, Laura Esserman, MD, MBA, Director of the Carol Franc

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has occurred with neuroblastoma in babies, where it is now recognized that neuroblastoma before the age of one is biologically different than that diagnosed at older ages and almost always regresses on its own.

The Case of Thyroid Cancer in Korea

Another example, said another keynote speaker, Hyeong Sik Ahn, MD, PhD, Director of the Institute for Evidence-based Medicine and Dean of the School of Public Health at Korea University School of Medicine, is the perceived thyroid cancer epidemic in Korea. The increase caused physicians to take a hard look at screening practices, which had resulted in a diagnosis rate of thyroid cancer in 2011 that was 15 times that observed in 1993.

The entire increase was subsequently found to be attributable to the detection of papillary thyroid cancer, and despite the dramatic rise in incidence, thyroid cancer mortality has remained stable.

Alarmed by the rise in incidence, eight physicians in March 2014 formed the Physician Coalition for Prevention of Overdiagnosis of Thyroid Cancer. The group sent an open letter to government health authorities and members of the media, calling attention to the rise in incidence and proposing that ultrasound screening be discouraged.

“Our approach to early detection has to evolve as our understanding of breast cancer biology evolves.”

—Laura Esserman, MD, MBA

Since then, a reduction of 35 percent in thyroid cancer surgeries has been observed, and—as a result of reviewing insurance claims—a 30 percent reduction in incidence has also been observed, Ahn said. The decline in surgery is not due to more conservative surgical practices, such as active surveillance, but rather to reduced use of screening and thus fewer diagnoses.

Reducing Unnecessary Prostate Cancer Screening

Kaiser Permanente, which serves about 10 million members in nine U.S. states and the District of Columbia, has taken steps to reduce unnecessary prostate cancer screening in older men, and a trend analysis presented at the conference showed the rate of such screenings dipping in all regions.

At the regional level the rate declined between three and 13 percent.

The Veterans Health Administration in the U.S. Department of Veterans Affairs, which treats some six million veterans in 150 hospitals and 800 affiliated outpatient clinics, has also taken steps to reduce overdiagnosis, reported Timothy J. Wilt, MD, MPH, Core Investigator with the Minneapolis VA Center for Chronic Disease Outcomes Research and Professor of Medicine at the University of Minnesota School of Medicine.

Reducing inappropriate PSA prostate cancer screening in men aged 75

or older has been one strategy to cut down on overdiagnosis. “Screening is a cascade of events, not just one test,” he said. “Screening is a double-edged sword: Less intensive screening is often of higher value than more intensive screening.

Recommended Strategies

Speakers recommended the following strategies as potentially helpful in reducing overdiagnosis:

- Arranging for a second opinion;
- Following clinical practice guidelines from professional societies;

- Wiser screening overall based on evidence-based risks;
- Participation in the American Board of Internal Medicine Foundation’s Choosing Wisely campaign;
- Having honest, personalized discussions with patients on the benefits and risks of screening and/or medical treatment, including active surveillance;
- Disseminating patient education materials that spell out the risks and concerns about overdiagnosis; and
- Creating computerized clinical decision support tools to help patients make informed decisions. ■