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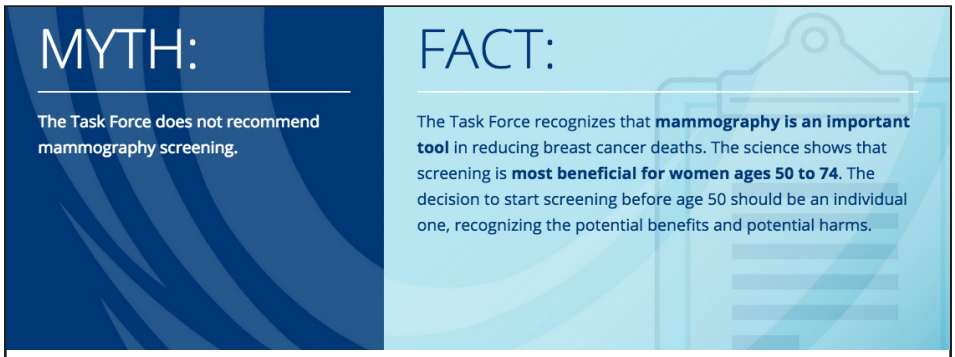

Foes Immediately Vow to Nullify Task Force Guideline on Mammography for Women 40-49

By Paul Goldberg

The breast cancer screening recommendations proposed by the U.S. Preventive Services Task Force earlier this week are basically unchanged from the 2009 version.

WARNING: a reader's yawn at this juncture would be misplaced.

The recommendations proposed and put in place five years ago were so politically radioactive that they could have jeopardized the passage of the Affordable Care Act.

Indeed, the ACA specifically excluded the task force's 2009 recommendation on mammography.

(Continued to page 2)

Mammography: When, Really, is the Right Time? And at What Cost?

By Matthew Bin Han Ong

As a firestorm ignites around the U.S. Preventive Service Task Force draft recommendation on mammography, researchers and advocates are grappling with the questions at the heart of the controversy:

• Should women start screening for breast cancer at age 40 or 50?

• What is the prevalence of false-positives and overdiagnosis in these age groups?

• What are the costs of harm?

(Continued to page 3)

Four Decades of Mammography Wars

The latest draft guideline by the U.S. Preventive Services Task Force is part of nearly a four-decade war over the appropriateness of screening women between the ages of 40 and 49.

In this war, Congress usually intervened, claiming that "common sense" dictates that mammography is efficacious in younger women. This war has often engulfed NCI.

(Continued to page 13)

Specialists, Lawmakers Say They Will Nix USPSTF Guideline

(Continued from page 1)

Immediately after the 2009 draft recommendation was published, then HHS Secretary Kathleen Sebelius in effect urged women between 40 and 49 to disregard the panel's evidence-based guideline. An amendment to the ACA, called the "Women's Preventive Health Amendment," finished the job of invalidating the guideline. (This made the ACA politically viable.)

Some folks in Congress launched efforts to eliminate funding for the independent USPSTF. Today, Congressional efforts to broaden the panel to include subspecialists and even the industry are ongoing.

The 2015 guideline, published April 20, resurrects the controversy—and if anything, the situation today has even greater thermonuclear potential: while the 2009 guideline is specifically excluded from ACA, the 2015 document isn't. At least not yet, some say.

Under the provisions of ACA, a low grade—in this case a "C"—for mammography screening among younger women could mean that private insurers wouldn't be obligated to cover mammography for women between ages of 40 and 49.

Will insurers be obligated to pay, or will they be allowed to cite USPSTF's recommendations as a basis for refusing to pay? Ultimately, the stakes are higher than breast cancer screening. If some of the USPSTF recommendations are to be disregarded while others get implemented, then why pretend that evidence-based medicine has a role in determining U.S. health policy?

"So why does it appear to be the situation in the ongoing polemic about breast cancer screening guidelines that an evidence-based approach is abandoned when it does not result in guidelines which are those which are not liked or welcomed?" said Peter Boyle, president of the International Prevention Research Institute, professor of global public health at Strathclyde University, and lead author of the State of Oncology 2013 report.

"Is this just a U.S. phenomenon?" said Boyle. "Guidelines for breast cancer screening in Europe have changed little in the last 25 years.

"Some things are clear," he said. "There is more to screening that finding more, smaller cancers. An effective screening test, within a screening program, needs to be shown to reduce mortality from that cancer without creating a large, false positive pool of patients. Lack of a consistent reduction in mortality from large trials, and a large over-diagnosis rate, has led to moves against the widespread use of PSA testing for prostate cancer."

Another "C"

The 2015 recommendations—again—give a "B" to mammography screening of women between ages 50 and 74.

For women between 40 and 49, "the decision to start screening mammography in women prior to age 50 years should be an individual one," the 2015 draft guideline states. "Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years."

The public comment period will end May 18. It is not known when the final recommendation will be published.

On April 20, Sen. Barbara Mikulski (D-Md.) sent a letter to HHS Secretary Sylvia Burwell, urging that the 2015 guideline be overruled in the same way as the previous version.

"We know that early detection of breast cancer offers women their very best chance at a cure and at survival," Mikulski wrote to Burwell. "Mammograms are essential for that early detection. I am requesting that your Department take swift action to reassure the American public that you will do everything within your power to ensure the continued availability of free mammograms for all women aged 40 and older.

"Further, should the USPSTF's recommendations be finalized, I would strongly urge that all appropriate actions be taken by the Department of Health and Human Services to ensure patients' previous access to breast cancer screening is not impeded, discouraged, or eliminated. Finally, should the draft recommendation

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be finalized, I will actively and aggressively pursue all legislative options available to ensure that women aged 40 and older are able to continue receiving free annual mammograms."

The letter is posted here.

Mikulski last month announced that she wouldn't seek reelection in 2016.

Efforts to defang the USPSTF have been renewed on the Hill.

The American College of Radiology and the Society of Breast Imaging, are supporting a bill called the USPSTF Transparency and Accountability Act of 2015 (H.R. 1151), which seeks to change the composition of the task force by including "individuals that collectively have appropriate scientific expertise, including in fields of health sciences research, health economics, health promotion, disease prevention, and clinical care."

Under that bill, USPSTF "shall include balanced representation of practicing primary and specialty care providers, patient and health care consumers, and relevant stakeholders from the medical products manufacturing community." The measure was introduced in the House of Representatives by Reps. Marsha Blackburn (R-Tenn.) and Bobby Rush (D-Ill.).

The task force now includes generalists, primary care physicians, epidemiologists, statisticians and other experts on preventive services.

The idea was suggested by a committee of the Institute of Medicine as a way to remove professional, financial and emotional conflicts of interest from the guidelines process. The process specifically allows the expert organizations to have the ability to communicate what they believe should be recommended and why.

The USPSTF's role is to serve as an objective grand jury.

The issue of mammography screening is even more complex because a recent study, published in Health Affairs, used real insurance billing data to quantify the cost of false positive mammograms and overdiagnosis (The Cancer Letter, April 10).

New Research Fuels Old Debate On Mammography Screening

(Continued from page 1)

The USPSTF draft recommendation, published April 20, comes on the heels of a controversial study which estimates that the U.S. spends $4 billion a year on unnecessary mammograms for women between the ages of 40 to 59.

The study was published in the April issue of Health Affairs. Titled "National Expenditure for False-Positive Mammograms and Breast Cancer Overdiagnoses Estimated at $4 Billion a Year," the study, by Kenneth Mandl and Mei-Sing Ong, uses expenditure data from a major U.S. health care insurer for 702,154 women in 2011 to 2013.

Of the $4 billion, $2.8 billion is attributed to false-positive mammograms, and $1.2 billion to breast cancer overdiagnosis. The study measures the rate of false positives at 11 percent and estimates overdiagnosis at 22 percent.

The study also showed that women in their 40s were 24 percent more likely to have a false positive than women in their 50s.

"The false positive is a mammogram result suggesting breast cancer, which subsequently is recognized to be normal," study author Kenneth Mandl, a professor at Harvard Medical School, said to The Cancer Letter. "Women who have this are exposed to additional diagnostic workup and psychological distress from being concerned about a cancer diagnosis for days or weeks.

"Plus, there are potential risks from diagnostic procedures or even other false positives happening or false negatives happening in subsequent diagnostic workup.

"The rate of this is very high. In our study, it was 11 percent, and that's consistent with prior literature."

A conversation with Mandl and Ong, a research fellow at the Boston Children's Hospital, appears on p. 7.

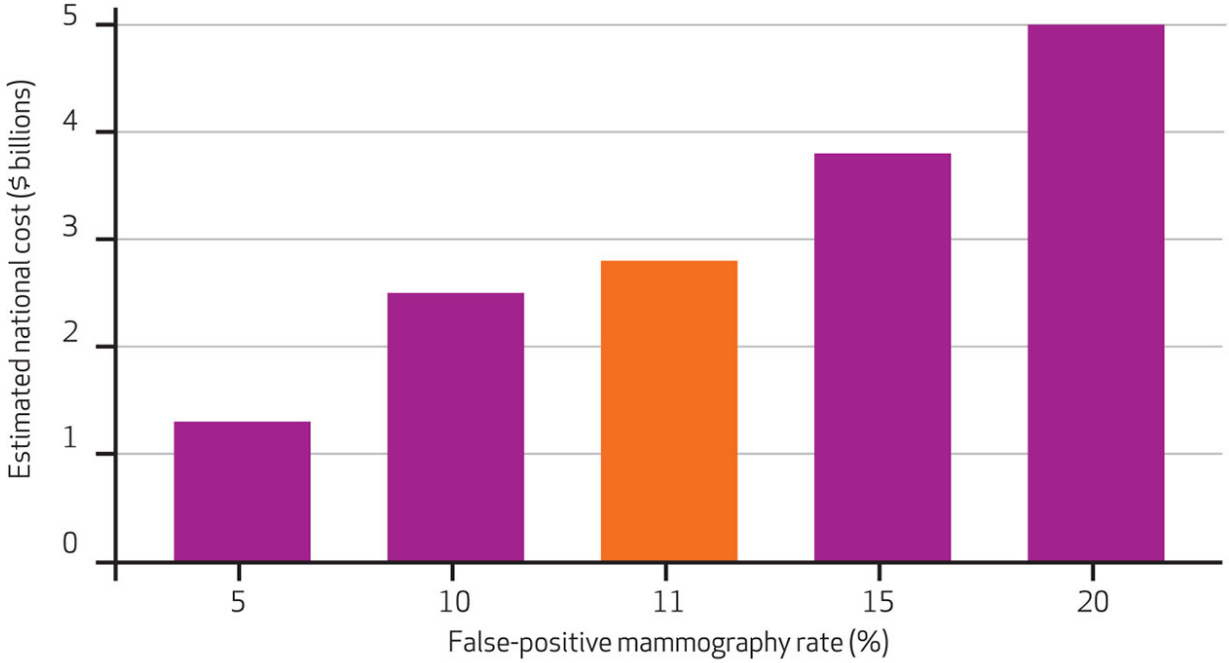
The task force's draft statement recommends a "C" grade for mammography screening for women between the ages of 40 and 49. If implemented, insurers would not be obligated to pay for mammography performed on younger women.

"The USPSTF concluded that the benefit of screening mammography outweighs the harms in this age range, but only by a small amount," the draft reads. "It is an acknowledgement that the balance of benefits and harms for any individual woman in this age group is a delicate one."

The public comment period will end May 18. It is not known when the final recommendation will be published.

EXHIBIT 4

Estimated Annual National Costs Of False-Positive Mammograms In The United States, With Varying False-Positive Rates, 2012–13



SOURCE Authors' analysis of data from a major US health care insurance plan and rates from the following: Elmore JG et al., Ten-year risk of false positive screening mammograms and clinical breast examinations (Note 7 in text); Brown ML et al., Screening mammography in community practice (Note 8 in text); Hubbard RA et al., Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography (Note 9 in text); and Christiansen CL et al., Predicting the cumulative risk of false-positive mammograms (Note 10 in text). **NOTE** In our study we used a false-positive rate of 11 percent to estimate the annual cost of false-positive mammograms (denoted here by the orange bar in the center).

Mandl: ACS Guideline = 61% False Positives

Costs associated with false-positive mammograms and breast cancer overdiagnoses appear to be much higher than previously documented, Mandl said.

"So if women are screened annually for a decade, as recommended by the American Cancer Society, 61 percent of women will have a false positive. The majority of women would be exposed to this potential harm of false positives following annual screening," said Mandl, also the Boston Children's Hospital Chair in Biomedical Informatics and Population.

The society's current guideline, established in 2003, recommends annual screening starting at 40. The task force's draft statement recommends screening every other year beginning at 50.

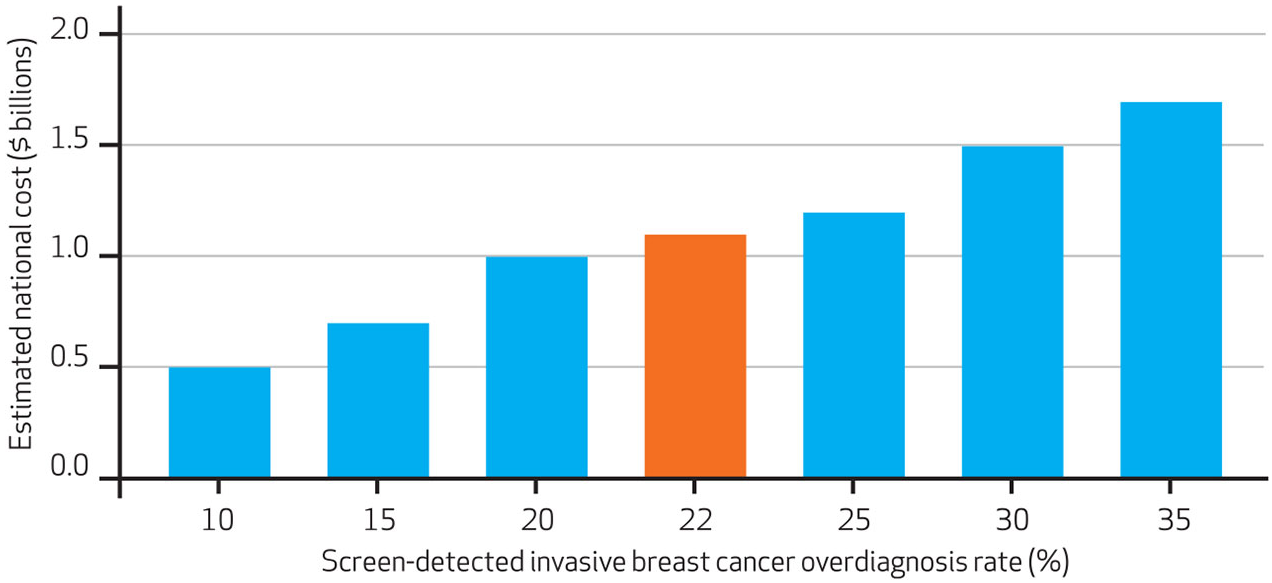
The study attempts to quantify extraneous costs generated as a result of false positives and overdiagnosis on the younger end of the screening spectrum, problems that the medical profession should try to minimize, Mandl said.

"The other aspect we looked at is much worse—and that's overdiagnosis, which is the diagnosis of lesions that are unlikely to become clinically important during the lifetime of the patient," Mandl said. "Lesions that look suspicious but aren't harmful, but nonetheless get treated with the full cancer treatment. This is estimated to be 20 and 30 percent or so of women treated on the basis of mammography. It's a concerning outcome."

The authors said their overdiagnosis rate, which

EXHIBIT 5

Estimated Annual National Costs Of Screen-Detected Invasive Breast Cancer Overdiagnoses In The United States, With Varying Overdiagnosis Rates, 2012–13



SOURCE Authors' analysis of data from a major US health care insurance plan and rates from the following: Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence (Note 2 in text); and Miller AB, et al. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study (Note 4 in text). **NOTE** In this study, we used an overdiagnosis rate of 22 percent to estimate the annual cost of breast cancer overdiagnoses (denoted here by the orange bar in the center).

Graph Source: Mei-Sing Ong and Kenneth D. Mandl, National Expenditure For False-Positive Mammograms And Breast Cancer Overdiagnoses Estimated At $4 Billion A Year, Health Affairs, 34, no.4 (2015):576-583

they borrowed from existing literature, is conservative.

"We used a conservative estimate of 22 percent," Mandl said. "Welch in JAMA and Bleyer in the New England Journal of Medicine in 2012 published comparable overdiagnosis rates. Bleyer's rate was closer to 30 percent, which would have increased the cost.

"So again, we took one number from the literature for overdiagnosis. Our number for false positives, which we measured, was consistent with the literature, and our costs are the actual costs paid out based on real data."

Wender: They Got It Wrong

Mandl and Ong's study contains "serious methodological flaws," said Richard Wender, chief cancer control officer at the American Cancer Society.

"Let me be really clear: I don't think that article should have or will have any impact on the task force, and it will not have any impact on our guidelines either," Wender said to The Cancer Letter.

According to Wender, the society has adopted a new process for developing cancer screening guidelines, and an update for breast cancer screening, authored by an independent committee, will be published later this year.

"[The committee] consists of a group of primary care, public health, and epidemiology experts, and we're going through a very similar process to what the Task Force did," Wender said.

Can the difference between the ACS and USPSTF recommendations be attributed to the use of different models?

"Not quite, although there is some truth to that," Wender said. "I'd like to point out that our last update for breast cancer guidelines was in 2003, so that was a long time ago."

Source: U.S. Preventive Services Task Force

Mandl and Ong's estimate for overdiagnosis is overblown, Wender said.

"Rather than doing their estimates with a broad range of published estimates of overdiagnosis, they picked one article, a 22 percent rate of overdiagnosis, which, the task force evidence review group said they don't have good confidence of what the true overdiagnosis rate is," Wender said.

"Therefore, there should have been a range of overdiagnosis estimates instead of a single number. There were other methodological flaws: they did their model assuming that all women were having mammography every year. They used the costs for annual mammograms although their tables showed that many women were screened less frequently. The actual cost numbers therefore are less."

The Ong and Mandl paper cite a 22 percent overdiagnosis rate, but acknowledge that estimates of overdiagnosis go up to 40 percent. This is provided in Table 5 of their paper, which estimates costs of overdiagnosis at 5, 10, 15, 20, 22, 25, 30, and 35 percent.

A conversation with Wender appears on p. 9.

Wender said his biggest concern about the Health Affairs paper is that the authors did not juxtapose their findings with the benefits of mammography.

"They did not do what I think is fundamentally necessary in deciding about screening, and that is looking at benefits," Wender said. "If you're going to do an article about costs, and all you do is publish the costs of the harms, and you do not publish anything about the benefits in real life, or about the direct or indirect financial benefits associated with reducing late-stage cancer with keeping people alive longer, particularly younger women—it's only an article designed to make a point about the high costs.

"They picked a high rate of overdiagnosis from a single study and there were simply some errors made in estimating the costs associated with screening.

"It should and did not have any impact on the task force's draft guideline, and based on what I know, I predict it will have no effect at all on the final guideline.

"I've never seen an article about costs where people can't debate the numbers, and this article is no different, but I think the far more important concern about this article affecting policy is that policy is separate from an individual decision, and has to take into account a balance of benefits and harms.

"That's how policy should be made, and it was obviously not the intent of the article to do that."

The authors, however, were right in stating that the sensitivity and specificity of mammography is lower for women in their 40s, Wender said.

"Because the rate of cancer is lower, particularly for women in their early 40s, any abnormality is more likely to be a false positive than a true positive simply because cancer is less frequent in younger women," Wender said.

Nevertheless, health care policymaking should prioritize benefits and risks over costs, Wender said.

"The other thing that is true, and is reflected in this article, but is not news, actually, is that cancer screening and certainly, mammography screening, is not cost-saving overall," Wender said. "The estimates do not suggest it is cost-saving to society and to health care.

"There is a real financial cost associated with screening, and thus, when making policy decisions about how we're going to spend our resources, you can only make that decision balancing the benefits and the risks. It's the only way to do it.

"There are many things in health care that are very costly, and are associated with very little benefit. The Choosing Wisely Campaign identifies a number of expensive diagnostic tests that are associated with little benefit.

"For mammography, we've seen a steady year after year after year drop in breast cancer mortality, and that

drop in mortality in the United States began exactly seven years after the ACS first recommended mammography. Up until then, there had been no drop at all."

Based on current evidence, women between the ages of 40 and 49 should engage in shared decision-making with their physicians to determine whether mammography is appropriate, Wender said.

"The key is tapping into a woman's values. So a woman that values the opportunity to prevent a premature breast cancer death and is willing to accept the risk of a false positive will opt to be screened in her 40s," Wender said. "The woman who values, primarily, the opportunity to avoid the mammogram experience, the false positive risk, and is willing to accept the small risk that she might experience a premature breast cancer death will opt not to be screened."

Mandl said the costs of harm must be weighed against the benefits.

"[Our study] doesn't tell us whether $4 billion is worth spending on mammography—that's not what we're trying to assess—$4 billion is a cost for something that clearly we would like to avoid, and that's false positives and overdiagnosis," Mandl said.

"That has to be balanced against the benefits."

Boyle: Mandl, Ong Used Solid Data and Estimates

The Mandl and Ong study provides important new data, said Peter Boyle, president of the International Prevention Research Institute, professor of global public health at Strathclyde University, and lead author of the State of Oncology 2013 report.

"This is a substantial contribution to the scientific-database which is currently being 'trashed' unfairly," Boyle said to The Cancer Letter. "It is analogous to 'playing the man' rather than 'playing the ball.'

"The authors identify over 700,000 women aged 40-59 who have a mammogram in 2012 and are followed for health care interventions and costs in 2012 and 2013. Real solid data here: not modeling estimates," Boyle said. "Their estimates for overdiagnosis of about 22 percent of all screen-detected invasive breast cancer were close to estimates done by the United Kingdom independent Panel, led by Sir Michael Marmot and published in Lancet (2012).

"The false positive rate of 11 percent which Ong and Mandl found has been repeatedly found by other major studies. In young women, they find false positive rates to be higher in younger women: Again, this is a common finding, mainly because breasts in younger women are radiologically denser. For the same reason, mammography is less sensitive in these young women, making screening poorly cost-effective in pre-menopausal women."

Changes to recommendations and guidelines need to be handled carefully, Boyle said.

"All recommendations must be evidence-based but the weight of evidence arguing for change needs to be substantial," Boyle said. "That adds to the polemic surrounding changes in recommendations.

"As we move forward there are still some issues gnawing away in the realm of breast cancer. Breast cancer programs have been effective at dramatically reducing the 'stigma' of breast cancer over the past decades.

"The whole package of lower stigma, increased awareness, mammographic screening and better treatments has been successful. We may not yet have succeeded in delineating the individual effects of each component but we can make further progress by continuing to reduce stigma, raise awareness, develop better screening tests, and discovering better treatments.

"With regard to screening for other cancers, it is intriguing that the most effective screening tests appear to be for cervix and colorectal cancer. For both forms of cancer, there are identified precursor lesions which can be detected by screening tests."

Conversation with The Cancer Letter

Mandl: Costs of Harm from Mammography Must Be Balanced Against Benefits

The U.S. spends $4 billion on unnecessary mammograms each year, according to a study published in the April issue of Health Affairs.

Titled "National Expenditure for False-Positive Mammograms and Breast Cancer Overdiagnoses Estimated at $4 Billion a Year," the study, by Kenneth Mandl and Mei-Sing Ong, uses expenditure data from a major U.S. health care insurer for 702,154 women in 2011 to 2013.

Of the $4 billion, $2.8 billion is attributed to false-positive mammograms, and $1.2 billion to breast cancer overdiagnosis. The study measures the rate of false positives at 11 percent and overdiagnosis at 22 percent.

"We're hoping that the stunning financial cost of this problem will help cast into greater belief the human cost—$4 billion tells you that it's a very large problem, that it's really happening at a massive scale," said Mandl, a professor at Harvard Medical School and the Boston Children's Hospital Chair in Biomedical Informatics and Population. His co-author, Ong, is a research fellow at the Boston Children's Hospital.

Mandl spoke with Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: *Why did you conduct this study, and what did you find?*

Kenneth Mandl: Some studies suggest that there is no difference in mortality between women screened and women not screened. In 2009, the U.S. Preventive Services Task Force advised against routine screening in women aged 40 to 49. In Switzerland, their medical board recently recommended ending mammography screening altogether.

In Europe and in the U.K., mammography is done generally no more than once every two or three years. The benefits have been called into question, because of several studies looking at the overall impact on cancer mortality.

We looked at two major problems that clearly do result from mammograms, and these are problems that one can have with screening tests in general, because screening tests are tuned to a certain accuracy, and you're going to have—in virtually every test—some false positives, and some false negatives. We looked at false positives and also overdiagnosis.

The false positive is a mammogram result suggesting breast cancer, which subsequently is recognized to be normal. Women who have this are exposed to additional diagnostic workup and psychological distress from being concerned about a cancer diagnosis for days or weeks. Plus, there are potential risks from diagnostic procedures or even other false positives happening or false negatives happening in subsequent diagnostic workup.

The rate of this is very high. In our study, it was 11 percent, and that's consistent with prior literature. So if women are screened annually for a decade, as recommended by the American Cancer Society, 61 percent of women will have a false positive. The majority of women would be exposed to this potential harm of false positives following annual screening.

The other aspect we looked at is much worse—and that's overdiagnosis, which is the diagnosis of lesions that are unlikely to become clinically important during the lifetime of the patient. Lesions that look suspicious but aren't harmful, but nonetheless get treated with the full cancer treatment. This is estimated to be 20 and 30 percent or so of women treated on the basis of mammography. It's a concerning outcome.

MO: *What was the public response to your work?*

KM: Overall, it's been very positive. I presented this at the National Press Club, and the group there was very receptive, asking very intelligent questions. It's clearly an important topic and a controversial issue with different viewpoints.

There is a sense among many women that it's important to be screened in order to protect oneself. We fully understand that and we understand a willingness to undergo some medical testing. The problem is that other studies have called into question the benefit. What we do here is to attach a cost to the harms.

We're hoping that the stunning financial cost of this problem will help cast into greater belief the human cost—$4 billion tells you that it's a very large problem, that it's really happening at a massive scale.

It doesn't tell us whether $4 billion is worth spending on mammography—that's not what we're trying to assess—$4 billion is a cost for something that clearly we would like to avoid, and that's false positives and overdiagnosis.

The problem is, as Europe and the USPSTF are concluding, that the benefits may not really be there in the way that we had hoped. Our study elucidates that there are $4 billion in revenue in the system. At any time you've got revenue attached to a current practice, it's going to be harder to make a change.

MO: *You mentioned in passing that the results of your study hold up against existing literature. Could you explain that in greater detail?*

KM: We measured false positives in a way that we're quite confident about. We looked at people who had a mammogram who had further diagnostic workup and who never received a diagnosis of breast cancer, and that 11 percent rate is very consistent with these other rates in the literature.

The overdiagnosis rate we borrowed from the literature—we used a conservative estimate of 22 percent. Welch in JAMA and Bleyer in the New England Journal of Medicine in 2012 published comparable overdiagnosis rates. Bleyer's rate was closer to 30 percent, which would have increased the cost.

So again, we took one number from the literature for overdiagnosis. Our number for false positives, which we measured, was consistent with the literature, and our costs are the actual costs paid out based on real data.

MO: *Where do we go from here? Who else should be listening, and where do you hope your study will have traction in the field?*

KM: It's a very good question: who really should make these determinations? Ultimately, I think most payers will continue to pay for screening with mammography for some time, so whatever the

recommendation will be, there'll often be a personal choice that's made.

It's going to be very important to try to explain to women what the risks and benefits truly are; even as you and I are discussing it right now, amongst ourselves, it takes 15 minutes to get through the numbers.

It's a lot of information to communicate, and in general, neither physicians nor patients are great at truly understanding risks and characteristics of screening tests.

It is key to ensure that patients being screened are the right patients. If you apply a screening test broadly across the entire population where a disease is relatively uncommon, you are more likely to get false positives. And if you apply a test to a population with a condition that's more prevalent, more likely in the first place, then the test is more likely to be a true positive.

Looking at the extremes, you can understand it. If you did a test in a population that for sure has zero breast cancer, and you got back a positive, it would definitely be a false positive, because there are no true positives in that population.

At the same time, if you did the test where 100 percent of the patients had breast cancer, every positive would always be a true positive.

The point here is that picking the right population to screen is doable, and you can enrich your population and screen women who are most likely to have disease—for example, women with a family history of breast cancer, women with genomic risk factors for breast cancer, women who might be harder to screen by self exam, women with obesity or very dense breasts who might have a harder time picking out a small lesion in a self exam—these are people who could be better candidates, or who are more likely to benefit from a mammography.

Selective screening, or risk-based screening is probably the better thing to do.

Mei-Sing Ong: Ultimately, whether or not to undergo breast cancer screening is an individual choice. However, the decision to screen should be based on informed decision on the benefits and harms of screening.

Right now, the majority of women, and some physicians, are not aware of the harms associated with mammography screening.

We hope our study will help bring them to light. More studies are needed to better understand who are most likely to benefit from screening.

Conversation with The Cancer Letter

Wender: Mammography Guidelines Should Balance Benefits and Risks, Not Costs

A controversial study on the costs of unnecessary mammography, published in the April issue of Health Affairs, contains "serious methodological flaws," said Richard Wender, chief cancer control officer at the American Cancer Society.

Titled "National Expenditure for False-Positive Mammograms and Breast Cancer Overdiagnoses Estimated at $4 Billion a Year," the study, by Kenneth Mandl and Mei-Sing Ong, uses expenditure data from a major U.S. health care insurer for 702,154 women in 2011 to 2013.

Of the $4 billion, $2.8 billion is attributed to false-positive mammograms, and $1.2 billion to breast cancer overdiagnosis. The study measures the rate of false positives at 11 percent and estimates overdiagnosis at 22 percent.

"Let me be really clear: I don't think that article should have or will have any impact on the [US Preventive Services Task Force], and it will not have any impact on [the American Cancer Society] guidelines, either," Wender said.

Wender spoke with Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: *It looks like we have new data on breast cancer false positives and overdiagnosis, and a new draft recommendation on mammography from the U.S. Preventive Services Task Force. What is the message here?*

Richard Wender: Here's the story with overdiagnosis. I think that we're in the early stages of understanding what overdiagnosis is, and in the very early stages of communicating to the public in a way that makes sense and that they can understand.

The first step is to have a definition that makes sense—two extremes and one in the middle—and I like the one in the middle. One extreme is a diagnosis of something that looks like a cancer under the microscope, but it has no biologic potential to progress at all. Even though it looks like cancer, it is completely benign in its behavior. It doesn't matter how long you live. It would never harm you.

At the other extreme—and I think this is the one that we should be really worried about in estimating overdiagnosis, but I've seen it used and it really does

concern me—is when you're diagnosed with a cancer, and a couple of years later, you die of another disease, for example heart disease. In some models, people are counting that as an overdiagnosis because you die of something else.

There's always going to be intervening causes of death before a cancer had a chance to harm you. By that definition, you're going to estimate the rate to be much higher than I think is legitimate or is helpful to people. Just to be clear, I'm not referring to the screening that takes place when a patient has a terminal condition—the potential for overdiagnosis is real in this instance, and this is a real concern since the evidence shows this kind of screening is taking place.

The definition in the middle is the most practical, which is, you're diagnosed with a cancer that is very unlikely to cause harm within an expected lifespan. For instance, you're diagnosed with a prostate cancer at an older age, but it takes 15 to 20 years to get to the point where it causes symptoms, but it's gone beyond your expected lifespan.

The problems come in measuring overdiagnosis. What the U.S. Preventive Services Task Force evidence review said, is that their confidence that there is overdiagnosis was high, but their confidence in estimating the magnitude of overdiagnosis was low.

Nevertheless, the task force picked a pretty high rate of overdiagnosis to use as their estimate of about 19 percent. And I did not see much differentiation between invasive breast cancer, for which the overdiagnosis rate likely is very low—more like 1 to 3 percent—and ductal carcinoma in situ, some of which biologically does not progress.

The report specifically says that there's a huge published range of overdiagnosis—everything from 0 percent to over 50 percent—and they picked 19 percent, which I believe comes from the Marmot report.

My estimate, based on my reading, is 1 to 3 percent for invasive, 20 to 50 percent for DCIS. Overall, it's probably like 10 percent, and if you eliminate DCIS, the rates are, in fact, very low.

MO: *What do we know about how people handle overdiagnosis?*

RW: Very little. The data that we do have is that people don't regret their decisions to be treated. People understand that they made a decision. They feel good that they found something early, and that they didn't die of that disease. They have no way to know particularly, if they have DCIS, if it would've progressed or not, at least given today's technology. They just make the decision that is right for themselves at the time.

I don't think we know the best way to communicate about overdiagnosis. What we do know about breast cancer screening and mammography, even from the very old, out-of-date randomized clinical trials conducted decades ago using old technology, is that it has at least a 20 percent rate of reduction in the risk of dying from breast cancer at virtually all ages.

If you look at the more recent observational trials of more modern mammography, the benefits are much higher than 20 percent. A more recent Canadian report comparing women who have been in their national screening program saw approximately a 40 percent reduction for women in every decade from 40 to 70 and over 30 percent for women in their 70s

So we know there are substantial benefits, and the real question is, how do we balance and judge those? I think women place high value on the opportunity to prevent premature breast cancer death, particularly in younger women, where the potential years-of-life-lost is very high.

I want to emphasize, for The Cancer Letter specifically, that the American Cancer Society has adopted a new process for authoring cancer screening guidelines. We published a paper in JAMA in 2011 about that, and we will be issuing an update for breast cancer screening guidelines this year using that completely new process, and that is a committee that's really walled-off from the rest of the American Cancer Society in many respects.

It consists of a group of primary care, public health, and epidemiology experts, and we're going through a very similar process to what the task force did, and we look forward to our recommendations being available later this year.

MO: *So you're saying that the estimates and opinions in this interview are solely yours, not the American Cancer Society's?*

RW: Yes. But many of my comments here are responding to the USPSTF draft statement and evidence review. And the report specifically states that their confidence about how much overdiagnosis occurs is low.

We truly don't know with what the rate is with any precision.

The evidence review from ACS is looking at the exact same questions, including the rate of overdiagnosis, and they will comment on both what the range of estimates is, and their confidence in those reports. They've been charged to do the same thing.

MO: *You mentioned that the benefit of breast cancer screening is a 20 percent reduction in risk of*

death from breast cancer? Is that risk relative, or is it absolute? What is the difference?

RW: Great point. That has a big impact on this issue of age-related recommendations. We have a chance with these new updated guidelines from the task force now and from ACS later in the year to really clarify this for the public. That will be a great opportunity because I think there's too much polarization.

I think many people have come away from the 2009 task force report thinking that mammography in their 40s didn't work, that mammography in younger women is ineffective. In fact, that's not the case, and the 2015 report makes that very clear.

Mammography is essentially equally effective, though slightly less sensitive in women in their 40s. But relative mortality reduction, is essentially the same, based on the trials at all ages, from 40 up to 60, and somewhat better from 60 to 69, after which we don't have trial data; there's no reason to expect that the mortality reduction in women older than 75 would be any less, depending, of course, on how long a woman lives.

The relative benefit is similar across all ages. What we're really talking about is absolute benefit: What makes a 40-year-old woman different from a 50-year-old woman? The answer is the risk of developing breast cancer.

Basically, starting in the 30s, a woman's risk of developing breast cancer goes up every year until she's in her 70s. If you screen people at very low risk of the disease, it becomes, in an absolute way, more likely that the only thing they could experience, is a harm, such as a false positive, and quite unlikely that they would experience a benefit.

I like to think that there are two kinds of threshold decisions regarding the benefit of screening for breast cancer at different ages. At what age is the cancer risk high enough to warrant a discussion about breast cancer screening, taking into account a woman's values?

The task force felt that that age is age 40. By 40, the risk is now high enough to warrant a discussion. It's not that women don't develop breast cancer at younger ages, obviously they do, but it's so infrequent that we would not screen them. By the way, the ACS's current guidelines say the same thing: start at 40.

Then a second age decision is made, and that is, at what age is the risk of breast cancer substantially higher so that the benefits substantially outweigh the harms. The task force said that that age is age 50—so that starting at 50 they recommend that women should be screened every other year.

The ACS's current guideline says that that age is 40, you should not only have the discussion, but you should be screened annually. And that's exactly the set of questions that our guideline committee is now considering.

The task force did mention that there is some benefit to annual screening, but again, when they balanced risk and harms, I'm not sure that their modeling was perfect, but remember when you move from annual to every other year, you will increase your false positive rate. It's not very likely that you will increase your overdiagnosis rate, though. More frequent screening will contribute to mainly more false positives, because you still would have found the cancer the following year.

The task force made a judgment for all ages: they felt that the incremental benefit of annual screening was not warranted due to the additional number of false positives.

MO: *Right, so how should clinicians and women start thinking about the 40 vs. 50 thresholds?*

RW: Your point is a good one—are clinicians really prepared to help women have a meaningful shared-decision discussion at age 40? I'm a family doctor, I'm not an oncologist, and I feel very confident that it's practical, it can be done, but I don't mean to imply that it's easy.

The key is tapping into a woman's values. A woman that values the opportunity to prevent a premature breast cancer death and is willing to accept the risk of a false positive will opt to be screened in her 40s. The woman who values, primarily, the opportunity to avoid the mammogram experience, i.e. the false positive risk, and is willing to accept the small risk that she might experience a premature breast cancer death will opt not to be screened.

MO: *The question therefore, from a statistical standpoint, is, based on the data that we have right now, is the absolute benefit for women in their 40s different from women in their 50s?*

RW: Yes, the absolute benefit is lower for women in their 40s simply because they are at lower risk of developing breast cancer.

MO: *Do you think you'd have the same degree of certainty in terms of the estimate of benefit in those two age groups?*

RW: Yes, you can have the same level of certainty of benefit at virtually every age until you get very old, then it gets trickier because we have less data there and life expectancy must be predicted. So, while all

groups would agree that the absolute benefit increases with age, they may differ in their estimates of the age-specific absolute benefit.

This is with the understanding that at no age do we have perfect certainty, because, the randomized trials, which might theoretically be the most useful data in the case of breast cancer, have been churned over for decades. We're not going to get any more useful data from randomized trials—I think everybody's accepted that we've learned what we can.

This is not a trivial point: the task force has dealt with that, as they have in many of their cancer screening guidelines, by relying more on modeling to project the value of current day mammography.

Our guideline process has specifically made the decision to look at models, but to get as much important data as we can from observational data and trends of modern-day mammography, and that could theoretically result in some difference in how we look at the overall evidence.

MO: *Do you mean that the difference in the models used by the task force and the ACS has accounted for the difference in the current recommendations?*

RW: Not quite, although there is some truth to that. I'd like to point out that our last update for breast cancer guidelines was in 2003, so that was a long time ago. I'm mainly referring to the process that our current guideline committee is using to provide evidence about models, but also about modern-day observational studies.

We've done updates on women at high-risk, we are not updating that guideline this year, we're only updating our guideline for average risk.

MO: *Let's talk about the recent paper published in Health Affairs, authored by Kenneth Mandl and Mei-Sing Ong. There's been a lot of debate around their findings—what do you take away from the results of that study?*

RW: I've done some interviews with the media on that paper, and let me be really clear: I don't think that article should have or will have any impact on the task force, and it will not have any impact on our guidelines either. There are a couple of reasons for that.

The task force is quite explicit in that they don't consider costs in doing their guidelines. Secondly, there were serious methodological flaws in that article, the main one being that, rather than doing their estimates with a broad range of published estimates of overdiagnosis, they picked one article—a 22 percent rate of overdiagnosis, which, the task force evidence review group said, they don't have good confidence of what the true overdiagnosis rate is.

So therefore, there should have been a range of overdiagnosis estimates instead of a single number. There were other methodological flaws: they did their model assuming that all women were having mammography every year. They used the costs for annual mammograms although their tables showed that many women were screened less frequently. The actual cost numbers therefore are less.

My biggest concern about the article is that they did not do what I think is fundamentally necessary in deciding about screening, and that is looking at benefits. If you're going to do an article about costs, and all you do is publish the costs of the harms, and you do not publish anything about the benefits in real life, or about the direct or indirect financial benefits associated with reducing late-stage cancer with keeping people alive longer, particularly younger women—it's only an article designed to make a point about the high costs.

They picked a high rate of overdiagnosis from a single study and there were simply some errors made in estimating the costs associated with screening.

It should and did not have any impact on the task force's draft guideline, and based on what I know, I predict it will have no effect at all on the final guideline.

I've never seen an article about costs where people can't debate the numbers, and this article is no different, but I think the far more important concern about this article affecting policy is that policy is separate from an individual decision, and has to take into account a balance of benefits and harms. That's how policy should be made, and it was obviously not the intent of the article to do that.

MO: *Did they get anything right?*

RW: There are some things that are accurate in that the sensitivity and specificity are a little bit lower for women in their 40s, and because the rate of cancer is lower, particularly for women in their early 40s, any abnormality is more likely to be a false positive than a true positive simply because cancer is less frequent in younger women.

I think the other thing that is true, and is reflected in this article, but is not news, actually, is that most cancer screening and certainly, mammography screening, is not cost-saving overall. The estimates do not suggest it is cost-saving to society and to health care.

There is a real financial cost associated with screening, and thus, when making policy decisions about how we're going to spend our resources, you can only make that decision balancing the benefits and the risks. It's the only way to do it.

There are many things in health care that are very costly, and are associated with very little benefit. The Choosing Wisely Campaign identifies a number of expensive diagnostic tests that are associated with little benefit.

For mammography, we've seen a steady year after year after year drop in breast cancer mortality, and that drop in mortality in the United States began exactly seven years after the ACS first recommended mammography. Up until then, there had been no drop at all.

It's impossible to differentiate how much of that year after year drop is due to better therapy versus earlier detection. It's clear that both are playing a role, but there is no better way to substantially eliminate the likelihood of dying from breast cancer than to find it very early before it has spread and involved lymph nodes.

I know that our guideline group is making an effort to look at the harms of later diagnosis other than just what reduction in mortality rates. That is occasionally missed when balancing benefits and harms, that there may harms associated with the need for more aggressive treatment.

This estimate of harm is challenging, and I think in cancer screening, we've not done a great job, in part because the evidence is hard to find, frankly, for estimating the harm associated with treating more advanced stages of the cancer.

MO: *Thank you for taking the time to do this interview. Did I miss anything?*

RW: I hope we didn't miss anything. I think in the year 2015, we're going to look back on this and we're going to say, "This is the year that some of the polarized discussions about mammography started to disappear, and this is the year we've started to create a productive pathway forward to help women and clinicians make the right decisions for each individual about mammography screening."

40 Years of Mammography Wars

(Continued from page 1)

This timeline appeared in part in the Nov. 20, 2009, issue of The Cancer Letter.

In May 1977, NCI first adopts guidelines for mammography for use in breast cancer screening (The Cancer Letter, May 13, 1977). This was not a guideline for all women, just those women under 50 who were participating in the NCI-American Cancer Society study called the Breast Cancer Detection Demonstration Project. Younger women in the study were to receive screening only if they had a previous history of breast cancer or a mother or sister with the disease.

Later that year, the very first NIH Consensus Development Conference examined the issue of screening mammography and whether to continue the BCDDP. The panel concluded, based on data from the study, that screening mammography should be available for women over 50. Women 40-49 with a personal history of breast cancer or whose mothers or sisters had breast cancer should continue to be screened within the study (The Cancer Letter, Sept. 23, 1977).

In 1987, the results of the BCDDP came in. Though it was not a randomized trial, the results seemed to infer that younger women would benefit from screening to the same degree as older women. About this time, NCI, ACS and about 18 other organizations got together to establish a consensus on screening mammograms.

The Health Insurance Plan of New York trial showed a 30 percent mortality reduction in women over 50, but could not demonstrate a benefit for women between 40 and 49.

Still, NCI, ACS and the other organizations recommended annual clinical breast exam beginning

THE CANCER LETTER won a 2014 Sigma Delta Chi Award for Public Service in Journalism from the **Society of Professional Journalists** on April 23.

The Sigma Delta Chi Awards is a national competition dating back to 1932. The award recognizes Matthew Ong's series "Power Morcellation: A Hazardous Practice" as the winner in the Newsletter category.

"This award recognizes a newsletter that renders outstanding public services through extensive coverage of an issue facing the community it serves," the description reads.

Ong's series, which includes an interview documentary, can be found here.

at age 40, with screening mammography at one- to two-year intervals; and beginning at age 50, annual CBE and mammography. The statement also advised all women to perform a monthly breast self-exam, and suggested "special surveillance" for women with a history of breast cancer or breast cancer in her mother or sister.

In 1988, a new analysis of the HIP trial, by Kenneth Chu, was published in the Journal of the NCI. Women screened at ages 40-49 and followed for at least 18 years after trial entry had 24 percent fewer breast cancer deaths than the controls. However, the benefit didn't show up until nine years later.

According to a 1988 story by The Cancer Letter on these results, "the researchers said they hope that this study will help settle the under-50 screening debate."

The results did strengthen what became known as the "consensus guideline," and though the guideline was not accepted by every health organization, it was publicized widely by NCI, ACS and the groups that signed onto it. Plastic shower cards with the mammography screening recommendations and pictures of how to perform breast self-exams became ubiquitous.

In 1992, the results of the National Breast Screening Study of Canada were published in the Canadian Medical Association Journal. This was supposed to be the trial designed specifically to answer the question about screening mammography for women in their 40s. The study showed that women 40-49 who received mammograms did no better than women were weren't screened. In fact, the trial found that the women who were screened did worse than the control group.

More advanced cancers were found in the screened group in the first round of screening than in the control group.

Radiologists claimed that this demonstrated that the Canadian trial was biased. Something must have gone wrong in the randomization, they said. Stephen Feig, of Thomas Jefferson University, and Daniel Kopans, of Massachusetts General Hospital and Harvard University, in a report for the American College of Radiology, identified all the things they found objectionable in the Canadian trial.

Letters and rebuttals between the Canadian investigators and Feig and Kopans, and others, filled various journals during 1992.

To deal with this imbroglio, NCI officials decided to hold a conference.

In February 1993, the NCI Workshop on Breast Cancer Screening developed a report that became known as the Fletcher report after the panel's chairman, Suzanne Fletcher of the American College of Physicians. This report didn't make any recommendation, but reviewed the available data.

For the 40-49 age group, "there is no reduction in mortality from breast cancer that can be attributed to screening," the report said. "There is an uncertain, and, if present, marginal reduction in mortality at about 10 to 12 years.

Only one study provides information on long-term effects beyond 12 years, and more information is needed." The report also called these 10-year age groupings "arbitrary and without biologic justification."

Radiologists attacked the report—and questioned Fletcher's qualifications. "Women and physicians should be aware of the fact that there are strong inferential data that screening can reduce mortality for women 40-49," Kopans wrote in a letter to The Cancer Letter.

"Inferential" benefit—rather than statistically significant benefit—was what NCI had based its original guideline on for women in their 40s. Many organizations, clinicians, and radiologists took the view that there was no need to change the guideline.

But maintaining the status quo didn't sit well with then NCI director, Samuel Broder. In his public remarks, he seemed to view it as a moral issue: How can you claim that screening mammography saves lives if you don't have statistically significant evidence that it save lives?

This represented a seismic shift at NCI. The institute was changing the rules of the game.

This change was alluded to when, in September 1993, the NCI Physician's Data Query database stopped referring to screening guidelines, instead issuing "summary of evidence statements" about cancer screening methods (The Cancer Letter, Sept. 17, 1993).

Having made that change, the institute had no choice but to back away from the 1988 guideline. The result was a brutal political battle.

In September 1993, Broder presented NCI's proposed revised statement on screening mammography to the National Cancer Advisory Board.

The board was informed rather late in the game about the change of rules. PDQ had already made its changes.

The proposed guideline recommended that women 40-49 "discuss with a health professional the advisability of screening with mammography, taking into account family history of breast cancer and other risk factors. NCI also recommends annual clinical breast examination as a prudent practice for this age

group" (The Cancer Letter, Sept. 24, 1993).

"Our job is only to convey scientific knowledge," Broder said. "The best course is to acknowledge where we are. We can't protect the public from the fact that science may change things."

But the NCAB wasn't ready to back the proposed new guideline, and instead passed a resolution on a 14-1 vote asking NCI to delay action on the guideline. The prevailing view was stated by then NCAB member Ellen Sigal. "If there is no agreement on the science, how can we change the policy?" she said. "I went to all of those meetings. I heard those scientists say, 'We don't know.' Then I heard the scientists and physicians say they will continue to get mammography for themselves and would have their family members get it. How can we possibly change the guidelines?"

Proponents of screening alleged that NCI had to toe the line because the Clinton health care reform plan didn't include a screening mammography benefit for women in their 40s. Some NCI officials were intimating behind closed doors to some participants that there was pressure from the administration to make the changes, perhaps as a way of trying to push the board to support the change.

In December 1993, NCI issued a "summary of scientific fact," not a guideline. The three-sentence statement: "There is a general consensus among experts that routine screening every one to two years with mammography and clinical breast examination can reduce breast cancer mortality by about one-third for women ages 50 and older. Experts do not agree on the role of routine screening mammography for women ages 40 to 49. To date, randomized clinical trials have not shown a statistically significant reduction in mortality for women under the age of 50."

In early 1994, NCI was called to answer for this at Congressional hearings. Several members of Congress believed NCI's actions confused women and took away hope, and they were eager to browbeat those Bethesda scientists. At one hearing, Rep. Edolphus Towns (D-N.Y.) called NCI racist, sexist, and callous. Rep. Bernie Saunders (I-Vt.) called for kicking the rascals out.

Broder stated at Congressional hearings that the change had nothing to do with the Clinton health reform plan, and that NCI's movement away from the 1988 guideline was set in motion the year before the Clinton plan emerged.

Meanwhile, ACS and the American College of Radiology and others acknowledged that the data aren't in. However, while waiting for conclusive data, it would be prudent health practice to screen, they said.

The pressure to reach a consensus, to speak in a single voice and "avoid confusion" continued.

In 1996, new data were coming out of trials in Sweden, claiming a mortality reduction for women 40-49. NCI's new director, Richard Klausner, said it was time to re-examine the 1993 statement.

Time for another conference. The Swedish data had not been published yet in scientific journals, but had been presented at an international meeting, just one step on the road to validation. Was the institute under political pressure to quickly change the statement back to supporting mammograms for younger women? Certainly, the lashing by Congress was a recent memory.

This time, in an attempt to head off accusations of institutional bias, NCI decided against sponsoring the necessary conference. Instead, NIH would hold a Consensus Conference with a panel not selected by NCI.

In January 1997, the NIH Consensus Conference statement said that the evidence was insufficient to determine the benefits of mammography among women aged 40-49. The panel recommended that women aged 40-49 should be counseled about potential benefits and harms before making decisions about mammography.

The statement didn't provide much further information. When the statement was released at the conference, even some scientists who had been neutral on the subject of screening for women in their 40s attacked it for not addressing the Swedish data in a more detailed fashion.

According to a story in The New York Times, Klausner came running out of the conference auditorium to use the telephone. Klausner said he was "shocked by the conclusions and disliked their negative tone."

Klausner later claimed he was misquoted, and actually had been shocked by the level of anger that erupted at the end of the conference.

Be that as it may, the quote, as well as Klausner's comments at the press conference after the meeting, served to immediately trample the panel's conclusions.

At the press conference, Klausner said: "I am concerned that women are not being given, with the report, all the evidence that they actually need.... [M]y evaluation is that these studies have reached a statistical significance and that there is now evidence that we didn't have previously."

As NCI distanced from the panel's report, the NCAB began work on a separate statement.

In February 1997, the Senate passed a "sense of the Senate" resolution in a 98-0 vote, urging the NCAB

to consider recommending screening for women 40-49 or to direct the public to consider guidelines issued by other organizations. NCI officials were brought to Congress again to explain why scientists can't agree.

Pennsylvania Sen. Arlen Specter, then the Republican chairman of the Labor, HHS appropriations subcommittee, held four hearings in four months on this issue. It seemed that members of Congress this time had determined that screening in younger women saves lives.

NCI's role should be to "help us get a clear message, tell us what the risks are, tell us what the advantages are. There is no question," she said at a hearing, "that the advantages outweigh the risks."

In March 1997, as Congress and the Clinton administration exerted pressure on the institute to act immediately, the NCAB endorsed screening mammograms for women 40-49 every one to two years if they are at "average risk" for breast cancer. In a demonstration of solidarity, NCI and ACS released a joint statement saying that the two groups agreed that screening women in their 40s is "beneficial and supportable with current scientific evidence."

In a White House press briefing, President Bill Clinton praised the NCAB's recommendations for providing "consistent guidance to women" (The Cancer Letter, April 4 and 11, 1997).

In November 2009, USPSTF published a screening guideline that gives a "C" to breast cancer screening for younger women (The Cancer Letter, Nov. 20, 2009).

HHS Secretary Kathleen Sebelius almost immediately rebukes the recommendation. "There is no question that the U.S. Preventive Services Task Force recommendations have caused a great deal of confusion and worry among women and their families across this country," Sebelius said in a statement Nov. 18. "I want to address that confusion head on. The U.S. Preventive Services Task Force is an outside independent panel of doctors and scientists who make recommendations. They do not set federal policy, and they don't determine what services are covered by the federal government." (The Cancer Letter, Nov. 20, 2009).

In a matter of days, the text of the one-page summary of USPSTF recommendations on the task force's website has been altered to clarify the recommendation against routine screening for younger women.

The clarification, set off in a pink box, quotes what appears to be a press interview by USPSTF Vice Chair Diana Petitti:

"So, what does this mean if you are a woman in your 40s? You should talk to your doctor and make an informed decision about whether a mammography [sic] is right for you based on your family history, general health, and personal values." The statement is dated Nov. 19, three days after the release of the guideline.

Though the clarification is consistent with the guideline recommendation, resorting to postscripts containing expert opinion is an obvious, embarrassing break with tradition for the task force, whose purpose is to rise above opinion of a single expert by relying on a panel of experts charged to apply pre-specified criteria for systematic, comprehensive review of scientific evidence.

As the controversy continued to develop on Capitol Hill, the Senate Dec. 3 approved an amendment that would give the HHS Secretary authority to cover additional preventive services for women and specifically nullify the breast cancer screening recommendations.

The amendment, introduced by Sens. Barbara Mikulski (D-Md.) and Olympia Snowe (R-Maine), covers a wide range of preventive services and doesn't mention mammography specifically. These services would make these services available without copayment. The measure passed 61-39.

The Mikulski-Snowe amendment was further amended by Sen. David Vitter (R-La.) to disregard "the current recommendations of the United States Preventive Service Task Force regarding breast cancer screening, mammography, and prevention shall be considered the most current other than those issued in or around November 2009."

Under the Vitter amendment, these recommendations would not be used in setting coverage requirements. The amendment was passed without a roll-call vote.

In other developments on Capitol Hill:

• Rep. Frank Pallone (D-N.J.), held a hearing of the Health Subcommittee of the House Committee on Energy and Commerce to get the task force to explain its recommendations.

• Sen. Tom Harkin (D-Iowa), chairman of the Senate Health, Education, Labor and Pensions Committee, is similarly planning a hearing. The investigation follows up on a letter from 22 members of the Senate, who claimed that the guideline "could prove devastating for women at risk of breast cancer" and urged Harkin to focus the investigation on the task force.

"The American people deserve to know more about how this task force came to its controversial findings," the senators wrote (The Cancer Letter, Dec. 4, 2009).

AACR Annual Meeting 2015

Baselga Becomes AACR President. Two SU2C Dream Teams Launched, And Multiple Award Winners Named

José Baselga was inaugurated as president of the American Association for Cancer Research for 2015-2016, during the association's annual meeting in Philadelphia.

Baselga is physician-in-chief and chief medical officer at Memorial Sloan Ketteri\ng Cancer Center in New York.

"It is an honor to serve as president of the AACR," Baselga said. "We are currently in the midst of a revolution in cancer research, where new technologies and therapies are being developed at a record pace. The AACR is uniquely positioned to advance the promise of precision medicine initiatives. As president, I am eager to work with the AACR community as a whole to integrate basic and clinical research, improve access to clinical trials, coordinate our regulatory policies, and increase our ability to collaborate on the many breakthroughs occurring in cancer prevention, detection, and treatment."

Baselga helped pioneer treatments for women with HER2-positive breast cancer. He conducted the initial clinical trial that demonstrated that patients with advanced HER2-positive breast cancer benefited from treatment with the anti-HER2 monoclonal antibody trastuzumab. His most recent focus in the laboratory and clinic is the identification of mechanisms of resistance to anti-HER2 agents and the clinical development of novel agents—including PI3-kinase inhibitors and antiestrogen therapies.

Baselga has been actively involved in the AACR for more than 20 years. Together with Lewis Cantley, Baselga is a founding editor-in-chief of Cancer Discovery. He has served as a member of the board of directors (2009-2012), and member of the editorial boards of Clinical Cancer Research and Cancer Prevention Research. In addition, Baselga has served on numerous committees, including: chair of the Clinical Trials Committee (2012-2013), chair of the Research Grant Review Committee (2009), member of the Landon Foundation-AACR INNOVATOR Award for International Collaboration in Cancer Research Committee (2006-2008), the Pezcoller Foundation-AACR International Award for Cancer Research Committee (2004-2005), and the AACR Award for Outstanding Achievement in Cancer Research Committee (2002-2003). He was inaugurated into the 2014 class of fellows of the AACR Academy. Additionally, he is a principal of the Stand Up To Cancer Dream Team, "Targeting the PI3K Pathway in Women's Cancers."

He is an elected member of the American Society for Clinical Investigation, the American Association of Physicians, and the Institute of Medicine. He has also served as a past president of the European Society for Medical Oncology and on the board of directors for the American Society of Clinical Oncology and the European Cancer Organisation.

Prior to becoming physician-in-chief and chief medical officer at Memorial Sloan Kettering Cancer Center, Baselga was the chief of the Division of Hematology/Oncology and associate director of the Massachusetts General Hospital Cancer Center, and professor of medicine at Harvard Medical School in Boston.

He was also the director of medical oncology, hematology, and radiation oncology and chairman of medical oncology service at Vall d'Hebron University and Hospital, in Barcelona, Spain, and professor of medicine at the Universitat Autònoma de Barcelona. He also served as a faculty member of the Breast/Gynecological Oncology Service at Memorial Sloan Kettering's Memorial Hospital.

Nancy Davidson, director of the University of Pittsburgh Cancer Institute and UPMC Cancer Center, was inducted as president-elect. Davidson is director of the University of Pittsburgh Cancer Institute and UPMC CancerCenter.

She is a breast cancer researcher whose work focuses on clinical and translational breast cancer research, cancer biology and treatment, and the role of apoptosis and mechanisms of epigenetic regulation of gene expression of the estrogen receptor alpha gene in breast cancer treatment.

Carlos Arteaga, professor of medicine and cancer biology at Vanderbilt University School of Medicine, associate director for clinical research, director of the Center for Cancer Targeted Therapies, and director of the Breast Cancer Program at Vanderbilt-Ingram Cancer Center, now serves as past-president.

Stand Up To Cancer announced two dream teams at the annual meeting of the American Association for Cancer Research, focused on ovarian and lung cancer.

Stand Up To Cancer and the American Cancer Society formed a $20 million dream team focused

on lung cancer, which they announced at the annual meeting of the American Association for Cancer Research.

Jeffrey Engelman, associate professor of medicine at Harvard Medical School and director of thoracic oncology at Massachusetts General Hospital Cancer Center, will be leader of the Dream Team. **Jedd Wolchok**, chief of the Melanoma and Immunotherapeutics Service at Memorial Sloan Kettering Cancer Center, will serve as co-leader. The project is titled "Targeting KRAS Mutant Lung Cancer," and it will involve researchers from eight institutions.

SU2C and ACS will each provide up to $10 million over the three-year life of the grant. Bristol-Myers Squibb will provide $5 million to SU2C for the dream team.

Principal investigators on the Dream Team include: **Pasi Janne**, Dana-Farber Cancer Institute; **Roy Herbst**, Yale Cancer Center; **Charles Rudin**, Memorial Sloan Kettering; **Julie Renee Brahmer**, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; **John Heymach**, MD Anderson Cancer Center; **Frank McCormick**, UCSF Helen Diller Family Comprehensive Cancer Center; and **David Gandara**, UC Davis Health System.

Andrea Stern Ferris, chairman and president of the LUNGevity Foundation, and **Jeffrey Wigbels**, a senior vice president at Morgan Stanley and a lung cancer survivor, will serve as patient advocates.

The team's approach will include working to define the most effective therapies to target KRAS and critical related biological pathways, targeting the immune system for the treatment of KRAS mutant lung cancers, and integrating targeted therapies with immunotherapies for these lung cancers.

The second dream team, focused on ovarian cancer, was formed by Stand Up To Cancer, the Ovarian Cancer Research Fund, the Ovarian Cancer National Alliance, and the National Ovarian Cancer Coalition.

Alan D'Andrea, co-director of the Gene Therapy Center at Dana-Farber Cancer Institute, and the Fuller-American Cancer Society professor of medicine at Harvard Medical School, will lead the dream team. Elizabeth Swisher, professor in the Department of Obstetrics and Gynecology at the University of Washington in Seattle, will be co-leader.

The organizations will devote $6 million over three years to a project entitled "DNA Repair Therapies for Ovarian Cancer." The team hopes to expand on recent clinical advances seen with olaparib and other PARP inhibitors in current clinical trials. The team will also focus on prevention and early detection.

The project will also involve researchers at Mayo Clinic; University of Chicago; MD Anderson Cancer Center; and Memorial Sloan Kettering Cancer Center. **Kathleen Gavin**, executive director of the Minnesota Ovarian Cancer Alliance; **Sue Friedman**, executive director of FORCE (Facing Our Risk of Cancer Empowered); and **Jamie Crase**, an ovarian cancer survivor, will serve as patient advocates.

The addition of the two teams brings the number of SU2C Dream Teams launched since the program's inception in 2008 to 16. The AACR will be responsible for administering the grant and providing ongoing scientific oversight to ensure that progress is made.

Mario Capecchi received the **Award for Lifetime Achievement in Cancer Research** for his work in the development of gene targeting technology.

Capecchi is the distinguished professor of biology and human genetics at the University of Utah School of Medicine in Salt Lake City, an investigator with Huntsman Cancer Institute, a Howard Hughes Medical Institute investigator, and a fellow of the AACR Academy.

His work has allowed researchers to analyze the specific function of a particular gene by investigating the biological repercussions of its absence. It has also proven to be a vital asset in the analysis of genetic mutations common in cancer patients. His work in this area was recognized in 2007 with the Nobel Prize in physiology or medicine.

Capecchi has also been involved in studies involving the Hox gene family. His studies of these genes have offered insights into the genetics of development within various organ systems, primarily the brain.

Capecchi has been recognized with numerous other awards, including the Pezcoller Foundation-AACR International Award for Cancer Research, the Wolf Prize in Medicine, the National Medal of Science, the Albert Lasker Award for Basic Medical Science, the Kyoto Prize in Basic Sciences, the Baxter Award for Distinguished Research in the Biomedical Sciences from the Association of American Medical Colleges, the Alfred P. Sloan Jr. Prize from the General Motors Cancer Research Foundation, the Gairdner Foundation International Award, and the March of Dimes Prize in Developmental Biology. He is also an elected fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science.

Philip Low received ninth annual **Award for Outstanding Achievement in Chemistry in Cancer Research**.

Low is the Ralph C. Corley distinguished professor of chemistry and director of the Center for Drug Discovery at Purdue University. He is also a founder and chief science officer of two biopharmaceutical companies, Endocyte Inc. and On Target Laboratories LLC.

His award lecture was titled "Ligand-targeted Imaging and Therapeutic Agents for Cancer."

Low is being recognized for his pioneering development of low molecular weight ligands to deliver attached therapeutic and imaging agents selectively into pathologic cells such as cancer cells. This targeted therapeutic approach improves potency and reduces toxicity. Currently, there are nine low molecular weight ligand-targeted drugs being tested in cancer clinical trials. One of these drugs uses folic acid to target the highly toxic chemotherapeutic agent desacetylvinblastine hydrazide to cancer cells bearing the folate receptor. Low's research on low molecular weight ligand-targeted therapeutic and imaging agents has yielded more than 40 U.S. patents or patents pending.

In 2011, the first fluorescence-guided surgery was performed on an ovarian cancer patient using the technology invented by Low. His achievements have been recognized by numerous awards throughout his career, including the Roland T. Lakey Award, the Mathias P. Mertes Award, the Morrill Award, the American Chemical Society's Award for Cancer Research (George and Christine Sosnovsky Award), the Watanabe Life Sciences Champion of the Year Award, and Brigham Young University's Distinguished Alumnus Award. He has also been elected to the National Academy of Inventors.

In addition to the AACR, Low is a member of numerous professional societies, such as the American Association for the Advancement of Science, the American Chemical Society, and the American Society of Hematology. He also serves as president of the Folate Receptor Society, as chair of multiple scientific conferences, and on the editorial boards of several journals.

Richard Pazdur received the **Public Service Award** in recognition of his leadership as director of the FDA Office of Hematology and Oncology Products.

On an annual basis, approximately 30 percent of all new drugs approved by the FDA are oncology products, and under his leadership, the office has approved many treatments for patients, such as the recent approvals of immune-checkpoint inhibitors, immune modulators, and many targeted therapies.

Pazdur was recently named one of "The World's 50 Greatest Leaders" by Fortune magazine.

He served as an oncologist, researcher, and teacher at Wayne State University before becoming a professor of medicine and assistant vice president for academic affairs at MD Anderson Cancer Center. He joined the FDA as the director of the Division of Oncology Drug Products in 1999 and was named director of the Office of Hematology and Oncology Drug Products in April 2005.

Margaret Foti, chief executive officer of the American Association for Cancer Research was recognized with the **Children's Champion Award** for her efforts in pediatric cancer advocacy.

The AACR's Pediatric Cancer Working Group presented her the award during the association's annual meeting in Philadelphia.

During Foti's tenure as CEO of the AACR, membership has grown from about 3,000 to 35,000 researchers, scientists, health care professionals and advocates. Of these 35,000 members, nearly 2,000 comprise the membership of the AACR Pediatric Cancer Working Group, which was established in 2011.

Foti leads the AACR's scientific partnership with Stand Up To Cancer. Most recently, she received the 2014 Ellen V. Sigal Advocacy Leadership Award from Friends of Cancer Research, the 2014 Morton M. Kligerman Visiting Professorship Award from the University of Pennsylvania, the 2013 Stanley P. Reimann Honor Award from Fox Chase Cancer Center, and the 2013 Distinguished Partner in Hope Award during the Annual Colorectal Cancer Conference hosted by the Abramson Cancer Center of the University of Pennsylvania.

David Baltimore presented the 11th annual **AACR-Irving Weinstein Foundation Distinguished Lectureship**. Baltimore is president emeritus and the Robert Andrews Millikan professor of biology at the California Institute of Technology.

Baltimore, a fellow of the AACR Academy, was recognized for his work in immunology, virology, and cancer research. His research efforts are focused on using gene therapy methods to treat cancer and diseases such as AIDS. Baltimore received the Nobel Prize in physiology or medicine in 1975 for his work on viral

replication and his discovery of reverse transcriptase. He went on to research recombinant DNA technology, including discovering the transcription factor NF-κB and the recombination activating genes RAG-1 and RAG-2.

Baltimore's lecture was titled "MicroRNAs, Leukemia, and Hematopoietic Stem Cells Homeostasis."

The lectureship was established in 2004. The recipient is selected by the AACR president and is not open to nominations.

The research in his laboratory is currently focused on the development and function of the mammalian immune system and using viral vectors to carry new genes into immune cells to increase the range of pathogens effectively fought by the immune system.

In 1996, Baltimore was appointed head of the NIH's AIDS Vaccine Research Committee. He was an early advocate of federal AIDS research and co-chaired the National Academy of Sciences Committee on a National Strategy for AIDS in 1986. Baltimore currently co-directs the Joint Center for Translational Medicine, a joint effort between Caltech and the University of California, Los Angeles.

Baltimore's honors include the National Medal of Science, the AMA Scientific Achievement Award, and the Warren Alpert Foundation Scientific Prize from Harvard Medical School. He is also an elected member of the Institute of Medicine, the American Academy of Arts and Sciences, and the National Academy of Sciences, as well as a foreign member of the Royal Society in the United Kingdom and the French Academy of Sciences.

Carl June was recognized by the AACR and the Cancer Research Institute with the third annual **Lloyd J. Old Award in Cancer Immunology**. June is the Richard W. Vague professor in immunotherapy at the Perelman School of Medicine and director of the Center for Cellular Immunotherapies at the University of Pennsylvania in Philadelphia.

June was honored for his contributions to cancer immunology, specifically efforts related to the development of chimeric antigen receptor T-cell therapy. He presented his lecture "CAR T cells: Can We Move Beyond B cells?"

June, senior editor of Cancer Immunology Research, has been recognized with the Taubman Prize for Excellence in Translational Medical Science, the Karl Landsteiner Memorial Award from the American Association of Blood Banks, the Steinman Award for Human Immunology Research from the American Association of Immunologists, the Richard V. Smalley Award from the Society of Immunotherapy of Cancer, the Paul Ehrlich and Ludwig Darmstaedter Prize (shared with James Allison), the Legion of Merit from the U.S. Navy, and election to the Institute of Medicine and the American Academy of Arts and Sciences.

Prior to joining the University of Pennsylvania in 1999, June had been a professor in the Department of Medicine at the Uniformed Services University of the Health Sciences. A graduate of the United States Naval Academy, June served as a Navy medical officer from 1975 to 1996.

Researchers from Memorial Sloan Kettering Cancer Center and the University of California, Los Angeles were honored with the ninth annual **AACR Team Science Award** for their work in androgen receptor inhibitors.

The team is composed of leader **Charles Sawyers**, director of the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center; **Howard Scher**, chief of genitourinary oncology service and D. Wayne Calloway chair in urologic oncology at Memorial Sloan Kettering; and **Michael Jung**, distinguished professor in the Department of Chemistry and Biochemistry at UCLA. Sawyers is also past-president of the AACR and a Howard Hughes Medical Institute investigator.

The team is being honored for their collective work in discovering and developing the novel antiandrogen enzalutamide (Xtandi) for the treatment of metastatic castration-resistant prostate cancer. After determining that AR overexpression was responsible for fueling the growth and survival of castration-resistant prostate cancers, the team used preclinical models to identify novel AR inhibitors that blocked the growth of tumors. These studies led to the clinical development of enzalutamide, which received FDA approval in August 2012, after a phase III trial showed that the drug significantly extended survival among patients with metastatic, chemotherapy-resistant, castration-resistant prostate cancer.

The AACR Team Science Award is supported by grants from Eli Lilly and Company. The winning team collectively receives a $50,000 prize.

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Donald Coffey received the **Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research**. Coffey, a fellow of the AACR Academy, is the Catherine Iola and J. Smith Michael distinguished professor of urology at Johns Hopkins School of Medicine.

He served as president of the AACR from 1997 to 1998. His research work focuses on the structure of the cell nuclei and the pathogenesis of prostate cancer. He is known for the discovery of the nuclear matrix and the fact that DNA synthesis occurs on this matrix. He characterized the first Dunning animal models, which are used to isolate tumor metastasis genes and design chemotherapy regimens in prostate cancer. Coffey was the first to establish methods to identify androgen-insensitive prostate tumors and to elucidate the mechanisms of clonal selection in this insensitivity. He has also worked on telomerase in prostate cancer and contributed to the first prostate cancer gene therapy trial.

In addition to serving as president, he has been a member of the AACR board of directors and Nominating Committee, co-chair of the Science Education Committee, program chair of the AACR Annual Meeting 1995, and a member of the Public Education Committee and Long-range Planning Committee, as well as associate editor of Cancer Research.

Coffey has served on the National Cancer Advisory Board, the board of directors of the National Coalition for Cancer Research, as president of the Society for Basic Urological Research, national chair of the National Cancer Institute's National Prostatic Cancer Program, and director of the Brady Laboratory for Reproductive Biology and the research laboratories in the Department of Urology at Johns Hopkins.

Coffey has been recognized with numerous other honors, including the St. Paul's Medal from the British Association of Urological Surgeons, the Achievement Award from the American Urological Association, the First Yamanouchi Award from the Society of International Urology, the Eugene Fuller Prostate Award from the American Urological Society, and the Falk Award from the National Institute of Environmental Science.

James Allison received the **Pezcoller Foundation-AACR International Award for Cancer Research** for his discovery that blocking cytotoxic T lymphocyte-associated antigen 4 signaling improves antitumor immune responses, as well as for his role in the development of the CTLA-4 inhibitor ipilimumab (Yervoy), which was the first of a new class of immune checkpoint inhibitors. Ipilimumab was approved as a treatment for metastatic melanoma by the FDA in 2011.

Allison is chair of the Department of Immunology, executive director of the Immunology Platform, associate director of the Center for Cancer Immunology Research, deputy director of the David H. Koch Center for Applied Research in Genitourinary Cancer, and the Lilian H. Smith distinguished chair of immunology at MD Anderson Cancer Center, and a Howard Hughes Medical Institute investigator. He is a fellow of the AACR Academy and a member of the AACR board of directors. He is also deputy editor of Cancer Immunology Research and scientific editor of Cancer Discovery.

Allison lecture was titled, "Immune Checkpoint Blockade in Cancer Therapy: New Insights, Opportunities and Prospects for a Cure." Allison is currently investigating additional mechanisms involved in T-cell activation and signaling pathways.

Allison's recent awards include the inaugural AACR-Cancer Research Institute Lloyd J. Old Award in Cancer Immunology, the AACR-G.H.A. Clowes Memorial Award, the Canada Gairdner Foundation award, the Breakthrough Prize in Life Sciences, the Szent-Györgyi Prize for Progress in Cancer Research from the National Foundation for Cancer Research, the first Tang Prize in Biopharmaceutical Science, the Lifetime Achievement Award of the American Association of Immunologists, the Centeon Award for Innovative Breakthroughs in Immunology, and the William B. Coley Award for Distinguished Research in Basic and Tumor Biology from the Cancer Research Institute. He has been elected to numerous societies, including the National Academy of Sciences, and is a fellow of the Institute of Medicine, the American Association for the Advancement of Sciences, and the American Academy of Microbiology.

Owen Witte was recognized with the 55th annual **AACR G.H.A. Clowes Memorial Award**. Witte is the founding director of the Eli & Edythe Broad Center of Regenerative Medicine & Stem Cell Research and distinguished professor of microbiology, immunology, and molecular genetics at UCLA.

Witte, who is also a Howard Hughes Medical

Institute investigator and an elected fellow of the AACR Academy, was honored for his contributions to the understanding of human leukemias, immune disorders, and epithelial cancer stem cells. His lecture was titled "Finding Therapeutic Targets for Aggressive Prostate Cancer."

The AACR and Eli Lilly and Company established the award in 1961 to honor G.H.A. Clowes, a founding member of the AACR and research director at Eli Lilly. Witte's work helped define tyrosine kinases as crucial drug targets in human disease. Most notably, he pinpointed the molecular consequences of the Philadelphia chromosome abnormality present in chronic myelogenous leukemia and related types of leukemia and defined the tyrosine kinase activity of the ABL gene product. These findings played a crucial role in the subsequent development of ABL kinase-targeted therapies, including imatinib (Gleevec), which remains the front-line treatment for Ph-positive CML.

More recently, Witte's work has focused on defining the epithelial stem cell populations that contribute to prostate cancer. He is currently using mass spectrometry approaches to identify kinases that could be potential therapeutic targets for human prostate cancer.

Witte has been recognized throughout his career with numerous honors. He has received the Nakahara Memorial Lecture Prize, the Cotlove Lectureship from the Academy of Clinical Laboratory Physicians and Scientists, the de Villiers International Achievement Award from the Leukemia and Lymphoma Society, the Warren Alpert Prize, and is elected member of the Institute of Medicine, National Academy of Sciences, and fellow of the American Academy of Arts and Sciences and the American Academy of Microbiology.

Lewis Cantley presented the **Princess Takamatsu Memorial Lectureship**.

Cantley, the Meyer director of the Sandra and Edward Meyer Cancer Center, the Margaret and Herman Sokol professor in oncology research, and a professor of cancer biology in medicine at Weill Cornell Medical College in New York, was recognized for his seminal contributions to the field of growth factor and oncogene signaling.

This lectureship honors his discovery of the phosphoinositide 3-kinase enzyme and his subsequent work delineating the PI3K signaling pathway. His research has shown that this pathway is commonly activated in cancer and has paved the way for the development of therapeutics aimed at inhibiting PI3K signaling.

His lecture was titled "Targeting PI3K for Cancer Therapy." Cantley is also chair of this year's AACR Annual Meeting Scientific Program Committee.

The AACR Princess Takamatsu Memorial Lectureship is presented to a scientist whose novel and significant work had or may have a far-reaching impact on the detection, diagnosis, treatment, or prevention of cancer, and who embodies the dedication of the princess to multinational collaborations. Her Imperial Highness Princess Kikuko Takamatsu was instrumental in promoting cancer research and encouraging cancer scientists. She became a champion for these causes following her mother's death from bowel cancer in 1933 at the young age of 43.

Cantley is a founding co-editor-in-chief of Cancer Discovery, a member of the AACR board of directors, an elected fellow of the AACR Academy, and a leader of the Stand Up to Cancer Dream Team "Targeting PI3K in Women's Cancers."

Cantley's has received the Canada Gairdner International Award, the inaugural Breakthrough Prize in Life Sciences, the H.C. Jacobaeus Prize, the Pasarow Award for Cancer Research, the Rolf Luft Award from the Karolinska Institute, the Pezcoller Foundation-AACR International Award for Cancer Research, and the Caledonian Prize Lectureship in Biomedical Science from the Royal Society of Edinburgh. Additionally, he is an elected member of the National Academy of Sciences and the American Academy of Arts and Sciences.

Christopher Vakoc received the 35th annual **AACR Outstanding Achievement in Cancer Research Award**. Vakoc is an assistant professor at Cold Spring Harbor Laboratory. The award is given to an investigator younger than 40 years of age to recognize his or her meritorious achievements within the field of cancer research.

Vakoc was recognized for his research on the basic molecular mechanisms that control leukemias, and the connection between epigenetic regulation and oncogenesis. His work led to the development of potential new therapeutic approaches that are currently being evaluated in early stage clinical trials.

His lecture was titled, "Chromatin Regulators as Cancer Dependencies."

Vakoc has been recognized with the "A" Award from Alex's Lemonade Stand, the V Scholar Grant from the V Foundation for Cancer Research, the Forbeck Scholar Award, the Sass Foundation

Fellowship, the Burroughs Wellcome Fund Career Award for Medical Scientists, and the Sass Foundation for Medical Research Fellow Award.

Lucile Adams-Campbell was honored with the **Minorities in Cancer Research Jane Cooke Wright Lectureship**.

Adams-Campbell is a professor of oncology, associate director of minority health and disparities research, and associate dean of community health and outreach at the Georgetown Lombardi Comprehensive Cancer Center. She was recognized for her scientific contributions in the area of cancer epidemiology and health disparities.

Her lecture was titled "A Prospective Approach to Breast Cancer Risk in Black Women: A View from Two Cohorts – WHI and BWHS."

Her research focus has been diseases that disproportionately affect African Americans, including breast, prostate, and colon cancers, and identifying ways to overcome health disparities through disease prevention. She leads the National Institute of Minority Health and Disparities Center of Excellence for Health Disparities. She also is the co-principal investigator of the Black Women's Health Study, which led to the identification of obesity, diet, and physical inactivity as factors influencing risk for diseases disproportionately affecting African-American women such as cancer, lupus, high blood pressure, and diabetes, as well as served as co-principal investigator of the Women's Health Initiative.

Additionally, Adams-Campbell served as principal investigator the NCI's Minority Based Community Oncology Program, which was implemented to improve the number of black participants in clinical trials. Her research is inclusive of clinical trials, cancer epidemiology and etiology, and lifestyle interventions.

Adams-Campbell is an elected member of the Institute of Medicine and has received gold medallions from both of her alma maters, Drexel University in Philadelphia, where she received her bachelor's and master's degrees, and the University of Pittsburgh.

Before joining the Lombardi Comprehensive Cancer Center in 2008, Adams-Campbell was director of Howard University Cancer Center. She is also a visiting professor of oncology at Johns Hopkins University School of Medicine in Baltimore, adjunct professor of epidemiology at the University of Pittsburgh, and adjunct professor of medical and clinical psychology at the Uniformed Services University of the Health Sciences.

Sara Courtneidge presented the **AACR-Women in Cancer Research Charlotte Friend Memorial Lectureship.** Courtneidge was recognized for her contributions to the current understanding of Src-family kinases, as well as her advocacy for women in science.

Courtneidge is a professor in the Department of Cell, Developmental and Cancer Biology at Oregon Health & Science University and a senior investigator for OHSU's Knight Cancer Institute. Her lecture was titled "Cancer Cell Invasion and Metastasis."

The lectureship was established in 1998 in honor of virologist Charlotte Friend, discoverer of the Friend virus, for her pioneering research on viruses, cell differentiation, and cancer. Courtneidge's research has focused on oncologic transformation, including her discovery that the RSV v-Src transforming protein and its cellular counterpart, c-Src, are plasma membrane-associated, anchored to the membrane via an N-terminal myristoyl group.

She discovered that the middle T antigen of polyomavirus is associated with c-Src, a finding that revolutionized the DNA tumor virus field. Courtneidge also found that c-Src is activated by association with the PDGF receptor tyrosine kinase, and is required for mitogenic signaling in a pathway that leads to c-Myc.

Recently, Courtneidge identified the Tks4 and Tks5 adaptor proteins as Src substrates and showed that they function through Nox-mediated ROS generation at the surface of tumor cells where they trigger formation of invadopodia, which secrete proteases essential for tumor cell invasion through normal tissue.

Courtneidge has served on the AACR board of directors, nominating committee, as program chair of the Annual Meeting 2003, and as a scientific editor of several journals. She is currently on the editorial board of Cancer Today. Courtneidge is also an adjunct professor at Sanford Burnham Medical Research Institute and the University of California, San Diego.

Mitchell Gail received the **AACR-American Cancer Society Award for Excellence in Cancer Epidemiology and Prevention.**

Gail, a senior investigator in the NCI Biostatistics Branch of the Division of Cancer Epidemiology and Genetics, was recognized for his statistical work in cancer research and development of cancer risk prediction models, in particular models for breast cancer risk projection.

Gail described in 1989 a statistical model that estimated the absolute risk for a white woman of a specific age with specific risk factors—age of first live birth, age of menarche, number of first-degree relatives with breast cancer, and number of previous breast biopsies—to develop breast cancer. The model, commonly known as the "Gail model," was the first cancer risk prediction model that could be applied in a generalized population.

The NCI's Breast Cancer Risk Assessment Tool, which is widely used in clinical settings, is an adapted version of the Gail model. Additionally, the FDA used this model to determine a five-year breast cancer risk cutoff for approval of tamoxifen for use as a chemopreventative in women aged 35 and older.

Gail has been honored with numerous awards throughout his career, including the Nathan Mantel Lifetime Achievement Award from the statistics in epidemiology section of the American Statistical Association, the PHS Distinguished Service Medal, the Distinguished Achievement Award from the American Society for Preventive Oncology, the National Institute of Health's Merit Award, and the inaugural Breslow Lecture. He has served on numerous journal editorial boards and society committees, and is a past-president of the American Statistical Association. Additionally, he has been elected to several societies, including the Institute of Medicine and as fellow of the American Association for the Advancement of Science.

Elizabeth Jaffee, deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, received the 20th annual **AACR-Joseph H. Burchenal Award for Outstanding Achievement in Clinical Cancer Research**.

Jaffee, recognized for her contributions to cancer immunology in both the pre-clinical and early clinical settings, is also the Dana and Albert "Cubby" Broccoli professor of oncology at the Johns Hopkins University School of Medicine and co-director of the Skip Viragh Center for Pancreas Cancer, the Gastrointestinal Cancer Program, and the Cancer Immunology Program and Immunology and Hematopoiesis Division.

Her lecture was titled, "Immunologic Treatments for Pancreatic Cancer: Current and Future Strategies."

Her research included testing one of the earliest therapeutic pancreatic cancer vaccines (GVAX) in 1997. She has also shown that mesothelin is a viable target for therapeutic vaccines and adoptive therapy for pancreatic cancer.

Jaffee recently led a phase II trial that showed that a GVAX prime and Listeria Monocytogenes vaccine boost improved overall survival for patients with pancreatic cancer; this approach was recently granted breakthrough status by FDA.

Jaffee is currently leader of the Stand Up To Cancer-Lustgarten Foundation Dream Team: Transforming Pancreatic Cancer to a Treatable Disease. The Dream Team is conducting combination clinical trials and establishing biomarkers of tumor microenvironment reprogramming. The trials focus on novel immune-suppressive pathways within the tumor, either in combination with a T cell-activating vaccine or chemotherapy.

Jaffee currently serves on the AACR board of directors, as chair of the Cancer Immunology Working Group, and as co-chair of the Immunology Program Committee at this year's annual meeting. Additionally, she is deputy editor of Cancer Immunology Research and has been active in AACR mentoring programs, including those as part of the Women in Cancer Research Working Group.

William Hahn received the 39th annual **AACR-Richard and Hinda Rosenthal Memorial Award.**

Hahn is chief of the Division of Molecular and Cellular Oncology, chair of the Executive Committee for Research, and director of the Center for Cancer Genome Discovery at Dana-Farber Cancer Institute.

He was honored for his contributions to the understanding of the mechanisms underlying cancer initiation, maintenance, and progression. He presented the lecture "Systematic Identification of Cancer Targets."

Hahn is a senior editor of Molecular Cancer Research, and an editorial board member of Cancer Research and Cancer Discovery. Additionally, he recently co-chaired the 2015 AACR Special Conference: Translation of the Cancer Genome.