

# THE **CANCER** LETTER

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## Appropriations

### **House Measure Would Eliminate AHRQ, Rescind PCORI, Cut Outcomes Research, And Halt NIH's Title 42 Hiring Program**

*By Matthew Bin Han Ong and Paul Goldberg*

A spending bill that cleared a House subcommittee eliminates the Agency for Healthcare Research and Quality, and moves the U.S. Preventive Services Task Force to the office of the Health and Human Services Assistant Secretary for Health.

The legislation—which passed through the Appropriations subcommittee on Labor, HHS, Education and Related Agencies July 18—is intended to halt the implementation of the Affordable Care Act, by rescinding previously allocated funds and prohibiting the use of any additional money to implement the law.

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## US Preventive Services Task Force

### **Fallout Over PSA Guidance Continues— Specialty Groups Dissent, Congress Attacks**

*By Paul Goldberg*

The American Society of Clinical Oncology earlier this week issued a “provisional clinical opinion” that recommends physicians discuss prostate-specific antigen testing with asymptomatic patients whose life expectancy is ten years or longer.

The guidance contradicts the recommendations by the U.S. Preventive Services Task Force, which gave routine PSA testing of asymptomatic men the grade “D,” which means that the task force has concluded that there is at least moderate certainty that the harms of doing the intervention equal or outweigh the benefits in the target population.

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## Conversation with The Cancer Letter

### **How ASCO's Guideline Differs—And Why**

The American Society of Clinical Oncology’s recommendation on screening for prostate cancer with prostate-specific antigen is slightly more positive about the test than the guideline written by the U.S. Preventive Services Task Force.

Nonetheless, the ASCO “provisional clinical opinion” blasts a hole in the established practice of including the PSA test in routine chemistry panels used by primary care physicians.

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## House Bill Seeks to Eliminate Evidence-Based Medicine Agencies

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Besides eliminating AHRQ, the agency that monitors the manner in which medicine is practiced in the U.S., the legislation stops all new hires under the Title 42 program at NIH.

The spending bill also eliminates all funding for Planned Parenthood, with the caveat that these funds could be restored should the organization agree to stop providing abortions.

The bill provides \$30.6 billion to NIH and \$5.066 billion to NCI for the next fiscal year—a flat budget for NIH and a \$1.25 million cut for NCI. Overall, the House version of the \$150 billion HHS spending bill is \$8.8 billion below the President's budget request.

The House appropriations measure for NIH falls \$100 million below the Senate Committee's recommendations, and NCI was given nearly \$20 million less in comparison, but the House specifically allocated \$8 million for repairs and improvements to the NCI facility in Frederick, Md.

The legislation includes \$175 million for the National Children's Study, \$488 million for Clinical and Translational Sciences Awards, and \$376 million for Institutional Development Awards programs.

The bill provides \$5.75 billion to the Centers for Disease Control and Prevention—a \$66 million increase of the current budget—and frees up an additional \$126.5 million for the CDC by reducing the ability of HHS to

divert funds away from CDC programs.

The measure authorizes NIH to collect third-party payments for the cost of clinical services that are incurred in NIH research facilities and that such payments shall be credited to the NIH Management Fund.

The NIH director is instructed to maintain an allocation of 90 percent of the appropriated funds to extramural activities, and at least 55 percent of the total toward basic science activities. No funds from institutes, centers, or Office of the Director accounts may be used for any economic research programs, projects or activities.

The subcommittee members voted 8-6 to approve the spending bill. The measure will now advance to the appropriations committee.

### House Bill: Title 42 Not to Be Used

At NIH, a large number of top officials, including all institute directors, are paid under the Title 42 program, which NCI Director Harold Varmus describes as an important component of his efforts to recruit staff ([The Cancer Letter, July 6](#)).

The bill's section on Title 42 follows: "Hereafter, the provisions of title II of the [Public Health Service] Act shall not be used as authority for appointment and compensation of continuing, full-time employees, including special consultant employees, of HHS, except with respect to direct scientific employees already receiving compensation under such provisions as of the date of the enactment of this Act.

"This section applies to both definite and indefinite appointments. The rate of base compensation to any direct scientific employee under such provisions is limited to no more than the rate of such compensation received by such employee in fiscal year 2012.

"This section does not apply to personnel of the Commissioned Corps or the National Health Service Corps of the Public Health Service."

In another highlight, the bill reads: "None of the funds made available in this title may be used, in whole or in part, to advocate or promote gun control."

Patient-centered outcomes research is verboten: "Notwithstanding any other provision of law, none of the discretionary funds appropriated by this Act may be used to support any patient-centered outcomes research."

The bill rescinds \$150 million in funds made available through the Patient-Centered Outcomes Research Trust Fund in fiscal 2013. Similarly, \$1 billion made available for the Prevention and Public Health Fund is rescinded.

## THE CANCER LETTER

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**Editor & Publisher:** Paul Goldberg

**Associate Editor:** Conor Hale

**Intern:** Matthew Bin Han Ong

Editorial, Subscriptions and Customer Service:

202-362-1809 Fax: 202-379-1787

PO Box 9905, Washington DC 20016

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## **The Vote to Eliminate AHRQ**

If the House subcommittee measure becomes law, AHRQ would cease to exist as of Oct. 1 of this year.

After the bill advanced to the full committee, Republicans said they sought to eliminate AHRQ purely in order to save money.

In addition to funding outcomes and disparities research, AHRQ operates the U.S. Preventive Services Task Force, a panel of independent experts who produce recommendations on screening tests.

Recent USPSTF recommendations on screenings for breast and prostate cancers caused some patient groups and subspecialties to call for a revamping of the task force to include specialists (see a related story on page 1).

AHRQ and its research programs are an important component of the Obama administration's health care plan, as it seeks to delineate the health practices that work from those that do not.

The agency's budget grew from \$372 million to \$611 million in 2011. Approximately 80 percent of the AHRQ's budget is invested in grants and contracts focused on improving health care. This isn't the first near-death experience in AHRQ's 20-year history.

In 1993, the agency, then called Agency for Health Care Policy and Research, focused on writing guidelines for the clinical management of acute lower-back pain, which was interpreted by back surgeons as an attack on back fusion surgery, one of the most productive cash machines in American medicine. Almost immediately, spine surgeons started to lobby Congress to eliminate the agency, and, in fact, a House bill sought to eliminate it.

The agency survived that time, although with sharply reduced funds.

History has been hard on science-based agencies in Washington.

In 1995, under the banner of Newt Gingrich's "Contract with America," Congress eliminated the funds for the Office of Technology Assessment. Critics on the Hill said that OTA had been duplicating the work of other agencies.

Others pointed out that OTA had spent over two decades making enemies by studying the the scientific feasibility (or lack thereof) of the Star Wars missile defense system, the dangers of climate change, and a variety of hot-button medical topics.

The House bill is available at: <http://appropriations.house.gov/uploadedfiles/bills-112hr-sc-ap-fy13-laborhhsed.pdf>.

## ***US Preventive Services Task Force* USPSTF, ASCO Differ On PSA: Who Gets to Start the Conversation?**

(Continued from page 1)

While the USPSTF grade applies to all men, ASCO's provisional opinion distinguishes between men with a life expectancy of 10 years or more from men with a life expectancy of fewer than 10 years. For men in the latter group, ASCO does not recommend PSA testing.

"For men with a shorter life expectancy, we agree that the risk of harms associated with PSA-based screening and subsequent unnecessary treatment likely outweigh the benefits," said Ethan Basch, co-chair of the ASCO panel, and associate attending oncologist and outcomes research scientist at Memorial Sloan-Kettering Cancer Center.

"But for men with a longer life expectancy, our assessment of the evidence shows the balance of risks and benefits is less clear, and that well-informed conversations between men and their physicians remain worthwhile about harms, potential benefits, and appropriate management strategies if prostate cancer is found."

The recommendation was printed in the *Journal of Clinical Oncology*, which ASCO publishes. The society also released a decision aid for weighing the risks and benefits of screening. Both are available at: <http://www.asco.org/pco/psa>.

The *Cancer Letter's* conversation with Basch appears on page 1.

The recommendation comes at a time when USPSTF is facing political backlash over the prostate cancer screening recommendations and its earlier and equally unpopular recommendation on mammography.

Pending measures of legislative retribution include an effort by House appropriators to eliminate the USPSTF's parent agency, the Agency for Healthcare Research and Quality. Under the appropriations measure marked up by the House Committee on Appropriations, the agency would be defunct as of Oct. 1, and USPSTF would be transferred to HHS.

Separately, other legislators are trying to defang the influential task force by making it include specialists and advocates in the panel, and to vet recommendations with affected subspecialty and advocacy groups. The measure, introduced by Reps. Marsha Blackburn (R-Tenn.) and John Barrow (D-Ga.) and titled the USPSTF Transparency and Accountability Act of 2012, is available at: <http://www.govtrack.us/congress/bills/112/hr5998/text>.

On top of that, a measure introduced in both the House and Senate would force the HHS secretary to establish an advisory council on prostate cancer to draft a plan for the development and validation of an accurate test or tests, such as biomarkers or imaging, to detect and diagnose prostate cancer. NIH would be just one participant in this group. The bills—S. 3345 and H.R. 6033—are posted at: <http://www.govtrack.us/congress/bills/112/s3345/text>. The Senate version was introduced by Sens. Barbara Boxer (D-Calif.) and John Kerry (D-Mass.) and the House version was introduced by Rep. Elijah Cummings (D-Md.).

Debate over screening and the future of USPSTF is important in part because the task force's recommendations figure into the Affordable Care Act, which mandates coverage for tests that have A and B grades, but is silent on coverage of tests flunked by the task force.

Recently, in a letter to a Congressional critic, HHS Secretary Kathleen Sebelius wrote:

"I recognize your concern that the Task Force's final recommendation on screening for prostate cancer could affect coverage of PSA tests under Medicare. While the Department has discretion to modify or eliminate coverage for the PSA test based on the Task Force's recommendation, I do not intend to eliminate coverage of this screening test under Medicare at this time. With respect to private plans, the Affordable Care Act permits plans or issuers to provide coverage for services in addition to those recommended by the Task Force. Plans and issuers can therefore opt to continue covering PSA screening."

The letter from Sebelius is posted at: <http://www.prostatecancerroundtable.net/wp-content/uploads/USPSTFSebeliustoBaca021412.pdf>.

### **ASCO's Provisional Clinical Opinion**

One of the more significant differences between the ASCO recommendation and that of USPSTF is the manner in which a conversation about PSA is initiated.

A doctor who follows the ASCO recommendation would start the conversation with a patient who, in his estimation, would live another decade or longer.

A doctor following the USPSTF recommendation would not bring up the subject of PSA screening at all.

"Neither one rules out getting a PSA on a man," said Barnett Kramer, director of the NCI Division of Cancer Prevention, who wasn't involved in the writing of the ASCO guideline. "The practical implications are, if you follow the task force guidelines, you need not bring it up spontaneously and discuss it with a man

unless they bring it up, because its use is discouraged in routine practice, whereas ASCO says you can be more active and discuss the pros and cons, but not encourage screening."

The American Cancer Society has no plans to review its current screening guideline.

"The difference between ASCO and ACS is that ASCO says that you should do the informed decision-making with every man who has a greater than 10-year life expectancy," said Otis Brawley, ACS chief medical and scientific officer. "The difference is that ACS doesn't say every man, and ACS implies that a doctor who doesn't think screening is a great thing doesn't need to bring it up. ASCO doesn't give the doctor that option."

Even with ASCO recommending discussion of PSA for some men, it's clear that no organization recommends that PSA be incorporated into panels of tests automatically offered by doctors.

"The practical implications are similar in that both the task force and the ASCO panel presumably would say that we should no longer incorporate PSA into these automatic testing panels in routine use," Kramer said. "That's an important point, since PSA has for years appeared on these routine chemistry panels, and that left men at risk for being tested even without their knowledge."

This point isn't explicitly reflected in the ASCO recommendation, "but the implication is that you don't do it to anyone without an open discussion, and if PSA is in an automated chemistry panel, it doesn't lend itself to discussion," Kramer said. "It's a very clear corollary."

ASCO says its provisional clinical opinions are intended to offer evidence-based clinical direction to physicians following the publication or presentation of potentially practice-changing data from major studies.

"As the organization representing physicians who counsel and treat men with prostate cancer, we see the impact of screening and treatment decisions every day, and felt it was our responsibility to conduct a rigorous analysis of the available data to help guide this very important decision for many men," said Basch.

"Our approach is a balanced one that takes into consideration the life expectancy of the patient as well as the values and preferences of individual men. We also advocate for the use of evidence-based decision aids, research to improve screening methods, and reduction of overtreatment of likely insignificant cancers."

The society's PCO states:

- In men with a life expectancy less than or equal to 10 years, it is recommended that general screening for prostate cancer PSA testing be discouraged. For

these men, the evidence of harm seems to outweigh potential benefits.

- In men with a life expectancy of greater than 10 years, it is recommended that physicians discuss with their patients whether PSA testing for prostate cancer screening is appropriate for them. PSA testing may save lives for this group of men, but is also associated with harms, including complications from unnecessary biopsy, surgery, or radiation treatment for cancers that may be slow-growing and not ultimately life-threatening.

- It is recommended that information written in lay language be available to clinicians and their patients to facilitate the discussion of the benefits and harms associated with PSA testing before the routine ordering of a PSA test.

The society said the guidance is based primarily on evidence from a high-quality systematic review of data by AHRQ, and was developed by a nine-member panel of physicians with expertise in medical oncology, uro-oncology, radiation oncology, prevention, screening and statistics, as well as a patient representative.

The list doesn't include generalists, who do most of the screening of healthy men.

While the USPSTF also based its recommendations on the AHRQ analysis, the ASCO panel considered longer-term, updated data from clinical trials, gave greater consideration to data in a sub-population of younger men, and weighed the impact of that analysis differently than the USPSTF—concluding that PSA testing may reduce the risk of death from prostate cancer for men with longer life expectancies.

The panel found that, while large clinical trials have found no reduction in overall mortality from routine PSA-based screening, the evidence is less clear in healthy men with life expectancies over 10 years, and found that this sub-population alone may have lower prostate cancer specific-mortality with PSA testing.

In particular, the PCO points to 11-year data from the European Randomized Study of Screening for Prostate Cancer, which found that PSA testing reduced death rates from prostate cancer by approximately 20 percent in a sub-population of more than 162,000 men between the ages of 55 and 69 years.

The PCO said that better evidence on PSA testing for prostate cancer screening is urgently needed, particularly for certain high-risk subgroups such as men with a family history of prostate cancer or of African-American descent.

The panel also noted the need for research on more accurate prostate cancer screening tests, including new

tests that can help doctors more accurately determine which prostate cancers are high-risk and require treatment and which can safely be monitored for signs of progression.

“Our critical review of the evidence, including data on younger subpopulations of men, shows that PSA testing should not be discounted,” said Robert Nam, ASCO panel co-chair and a uro-oncologist at the Odette Cancer Centre at the University of Toronto.

“We recognize that many want this debate settled, and want the answer to be clear-cut. But it isn't. Until it is, we think physicians and men with longer life expectancies should be aware of the full scope of evidence on PSA testing for prostate cancer screening so they can make informed and shared decisions about the right course of action. Our goal is to help ensure that PSA testing is used intelligently and selectively, by testing and then treating only appropriate patients.”

ASCO's decision-making tool explains available data and important considerations about PSA testing in lay language and in a format men can use to discuss testing with their physicians. The decision aid is divided into two sections:

- Learning the risks and benefits of your options, with your doctor: This section summarizes data from the ERSPC trial, providing detailed pictographs and explanations of the results. This trial was cited because it was one of the largest and highest-quality trials. The section doesn't include the results of the PLCO trial, which was negative.

- Thinking through the decision, on your own: This section provides a detailed list of decision options regarding whether to undergo, delay or forego PSA testing; poses important questions for men to consider; and features a detailed decision-making table that helps men rank their values, preferences and concerns about PSA testing and potential implications.

### **The 10 Year Cut Point and Implications of PIVOT**

Kramer said the ASCO recommendation may be hard to implement because it requires doctors to estimate how long their patients are likely to live.

“They have given advice that's hard to put into practice,” Kramer said. “It's very difficult for any physician to talk to a patient and say, ‘Look, in my estimation you are not going to live 10 years.’ And physicians notoriously overestimate life expectancy anyway.”

Also, the 10-year life expectancy cut point, which has figured in other guidelines, isn't prospectively tested in the randomized trials, Kramer said.

“There isn’t strong evidence that allows you to make the cut point,” he said. “You can’t look at any of the randomized trials and get that 10-year cutoff. That’s an extrapolation based on the panel’s consensus rather than clear evidence that arises from clinical trials.”

The New England Journal of Medicine published the results of the Prostate Cancer Intervention versus Observation Trial July 19, which randomized 731 men to radical prostatectomy or observation, finding no difference in all cause or prostate cancer mortality.

The trial was not powered to detect a small difference in outcomes, but would have detected a large difference.

“I would say that PIVOT is good enough to tell me that if radical prostatectomy does save lives, it is a relatively small number, and at a cost of substantial morbidity,” said Kramer. “In the aggregate, the task force came to its conclusion based upon what is known about the balance of risks and benefits irrespective of the somewhat arbitrary cut point of 10 years life expectancy.”

PIVOT has obvious implications for screening, Kramer said.

“This is the first time radical prostatectomy has been directly compared to watchful waiting in the screening era and in our own medical setting, and in order for screening to work, it must be linked to effective therapy,” he said. “This study calls into question how confident we can be that there is effective therapy for screen-detected men.”

ACS’s Brawley said that, nuances aside, ASCO’s recommendation is largely consistent with that of other organizations.

“It’s important to realize that there are now six organizations that in their published statements say that there is a question mark as to whether PSA screening saves lives and that there is definite evidence that PSA causes harm,” Brawley said, referring to the recommendations of the National Comprehensive Cancer Network, the European Urology Association, the American Cancer Society, the American Urological Association, ASCO and USPSTF.

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“Every one of them says there is a problem with this test,” said Brawley. “Not a single one of them says they recommend the test, but the task force is so bold as to say they recommend against the test. And that’s the way people ought to look at it. Everybody is in the same ballpark.”

“What this should be is the end of mass screening, screening at the mall, in the van, at the grocery store parking lot, at the church.

“All that kind of stuff ought to stop.”

*DISCLOSURE: Paul Goldberg and Otis Brawley are co-authors of HOW WE DO HARM: a Doctor Breaks Ranks on Being Sick in America, a book published by St. Martin’s Press.*

### Conversation with The Cancer Letter **PSA Shouldn’t Be Included In Blood Chemistry Panels**

(Continued from page 1)

“People often say there is no harm to the patient of adding on an extra test for PSA, using blood already drawn for other reasons,” said Ethan Basch, co-chair of the panel that developed the ASCO recommendation. “But in fact there are many downstream consequences of doing a test, and so it shouldn’t be automatic.

“Getting a test should be discussed, because it does carry with it potential harm. In the United States, there are many men who are older, who have a low-grade cancer that will never become clinically meaningful for them,” said Basch, associate attending oncologist and outcomes research scientist at Memorial Sloan-Kettering Cancer Center. “Many of these men wind up getting biopsies or even prostatectomies, because it’s hard for them and their doctors to live with the knowledge of a cancer inside them, even if it’s indolent.”

Basch discussed the ASCO recommendation with The Cancer Letter’s editor, Paul Goldberg.

**PG:** So, how are your recommendations different from all the other recommendations?

**EB:** I can speak best to our own recommendations, then will comment on similarities and differences from others, particularly the U.S. Preventive Services Task Force’s recent recommendation.

The ASCO recommendations are born out of a rigorous analysis of existing data, including updated results and subgroup analyses, with attention not only to screening trials but also to studies evaluating treatment for localized prostate cancer—including the recently reported PIVOT trial.

Another feature of our approach was a multidisciplinary expert panel including clinicians

and outcomes researchers, statisticians, trialists, and patients—with an emphasis on methodology. In the end, our recommendation is similar in many ways to the USPSTF, with a particular nuanced difference.

For older men or those with a shorter life expectancy—10 years or less—research suggests that harms from the downstream consequences of PSA screening outweigh the benefits, because men who might undergo an intervention for localized cancer would not live long enough to experience the benefits, but would likely experience adverse effects.

For men who are younger and with a longer life expectancy—more than 10 years—the literature shows survival benefits. But there are still real harms related to biopsy, surgery, or radiation and far too many men undergo the latter procedures unnecessarily—so called *overtreatment*. The balance between harms and benefits for these men is close and comes down to personal values and preferences. This is why ASCO recommends an informed discussion about PSA screening for younger men and has provided an evidence-based decision aid alongside the recommendations.

Beyond the ASCO recommendations, and this is my own impression now, emerging evidence suggests a potential future screening and treatment strategy for these younger men. This would start with an in-depth discussion of potential harms and benefits based on the science. Then, for those who opt for screening and screen positive for prostate cancer, a risk-based algorithm can be used based on factors like PSA value and Gleason grade where men with lower risk cancers enter a surveillance program while those with intermediate risk cancers are considered for surgery or radiation. PIVOT and the Scandinavian treatment studies support this approach.

I think we have a real opportunity to shift the risk-benefit profile of prostate cancer screening. We can optimize our strategy so that the benefits are extended to those who actually can benefit and not to those who won't, and we can focus on minimizing harms to the best extent possible—both by avoiding procedures in men who don't need them and through treatment innovations that minimize harms.

The nuanced difference between the USPSTF and ASCO recommendations is that ASCO states that for those men who are younger and have a longer life expectancy, a discussion should be offered—a discussion of the scientific evidence in understandable form such that men can really understand the science behind their decision—for example using the plain-language ASCO decision aid. The task force recommendation, as

I interpret it, is slightly different. It suggests that PSA testing should not be offered to any men including this younger cohort, however, if it is going to be considered, then there should be a discussion as I have laid out. So it is a nuanced difference, and actually is quite similar.

**PG:** The question is, who starts the conversation? Following ASCO's guideline, the doctor starts the conversation. Following USPSTF, the conversation can be started by the patient—maybe.

**EB:** I think that's one way to interpret the difference.

I can't speak for the intent of the task force. ASCO guidelines are created for a target audience of practitioners, and the recommendation here is to offer a discussion of PSA screening to younger men. We're providing practitioners and patients with support materials for this discussion which we hope will be refined and tested over time.

**PG:** Where does this 10-year life expectancy thing come from? That cut point is not in randomized trials, it's in some recommendations, of course, but can you actually look at somebody and say, you've got 10 years in you?

**EB:** Well, as with everything in medicine, we do the best we can towards informed decision making based on data but of course on a case-by-case basis the situation for an individual man is unique.

Where the number comes from, to answer your question, is that the age 75 is commonly used as the cut-off in trials and has been evaluated in analyses of the relationship of age to outcomes. If you look at life expectancy tables in the U.S. from the Social Security Administration, men who are between 75 and 77 or so have a 10- to 11-year life expectancy.

However, that's all comers. Comorbidities can substantially affect life expectancy. There was discussion during the development of the ASCO guideline whether we should use an absolute age—i.e. 75—or if it should be based on life expectancy, or if we should say both. Ultimately we decided to use a 10-year life expectancy with a recommendation of using a life expectancy calculator, and we provide a URL for the Social Security Administration calculator in the guideline itself, although there are others out there.

We don't particularly endorse one or another. If somebody goes to the Social Security calculator and plugs in ages looking for a 10-year life expectancy, they'll get around age 75 to 77 for a healthy man. But if a gentleman before me has a lot of other conditions, I become concerned that he may not live long enough to reap the benefits of screening, so I'd like to have another

way to consider the risk-benefit, and that's where the 10-year life expectancy comes in.

So it's a combination of data and practical, clinical judgment around how to figure out to our best ability who is going to benefit from this and who's going to face harm, so that's where that comes from.

**PG:** If the decision to be screened or not be screened has to arise from a conversation, does that mean that these automatic panels of blood tests should not be used anymore? Now, often, blood gets drawn and—boom—the patient gets his PSA score?

**EB:** Well I think that's a larger issue, and I think you actually allude to two different areas that are probably worth talking about.

First, it is common that a panel of tests is sent at doctor visits that may or may not be clinically meaningful and there really needs to be a rational scientific basis for tests being sent.

I think the second area you bring up is related to shared decision-making, consent, communication—talking about what's being evaluated and why it's being evaluated.

The latter is an important take-home message of the PSA screening debate—people often say there is no harm to the patient of adding on an extra test for PSA, using blood already drawn for other reasons. But in fact there are many downstream consequences of doing a test and so, it shouldn't be automatic.

Getting a test should be discussed, because it does carry with it potential harm. In the U.S., there are many men who are older, who have a low-grade cancer that will never become clinically meaningful for them. Many of these men wind up getting biopsies or even prostatectomies, because it's hard for them and their doctors to live with the knowledge of a cancer inside them, even if it's indolent.

An additional challenging issue the PSA debate has brought up is the problematic regulatory framework in the U.S. around screening and diagnostic testing, and the ease with which a new test can come on the market when it's unproven. This is what happened with PSA. PSA started being widely used and reimbursed for screening without proven clinical benefit. And today there are thousands of new tests being developed and marketed all the time and they aren't required to go through such scrutiny either.

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So today we face a real risk that the next PSA debacle is around the corner, particularly with genetic testing. I would argue there needs to be additional funding and resources to the FDA for overseeing the development and clinical validation of these assays.

**PG:** Or for the scientific community to come up with better ways to evaluate them up-front.

**EB:** Absolutely.

**PG:** Because that's really the bigger problem—the regulatory part of it is downstream, right?

**EB:** I completely agree, but there's often no downward pressure on the developers of these assays to do anything but obtain CLIA certification. There needs to be a whole framework around how these tests are developed and then regulated and then reimbursed, based on value to the patient.

**PG:** Of course, the results of PIVOT were published today. Here is the question they raise: what's the use of a detection modality if it's not connected to an effective treatment and here is something that doesn't have an effective treatment?

**EB:** I think the results of PIVOT are useful to this debate and are supportive of the ASCO recommendation as well as the recent NIH consensus recommendation about active surveillance. If you look at PIVOT subgroup analyses, the results support the notion that men with a low-risk localized cancer based on PSA and Gleason grade will live a long time despite their cancer and likely could go into an active surveillance program.

But men with an intermediate risk tumor would likely benefit from having an intervention.

This supports the overall screening and treatment strategy I described earlier. Now of course, this strategy needs to be prospectively evaluated, but to me that's the take-home of PIVOT and I actually see it as a strong complement to the ASCO recommendations.

**PG:** I should probably ask you this question as Ethan Basch, as opposed to as ASCO, so if you can just sort of change hats.

Today, a subcommittee of the appropriations committee marked up a bill that will eliminate the Agency for Healthcare Research and Quality and move USPSTF to the office of the HHS Assistant Secretary for Health, where it may not be quite so shielded from political interference. This is a scary time, in some ways, for those who believe in evidence-based medicine, for example, you.

**EB:** It would be a disaster to impair the work of AHRQ. AHRQ's work has led to enormous strides in our understanding of what patients and practitioners

face in everyday decision making about health.

Health care is incredibly complicated, people face difficult decisions every day. To impair our ability to interpret knowledge about science and medicine to aid these decisions shows a fundamental lack of understanding about how health care works, and about what information patients and practitioners need.

Any patient who goes to a doctor when facing a decision wants to know, “how am I going to feel with this treatment; how might I benefit from this treatment; what side effects might I experience; how would it affect my family if I make a certain decision; what has it been like for patients like me.” Parents want to know if a treatment is likely to benefit or harm their child and the only way to answer these questions is with trustworthy information and rigorous methodology, and that information comes from the interpretation of science. And that is the fundamental basis of agencies like AHRQ and the Patient-Centered Outcomes Research Institute.

Most of the research about PSA is technically comparative effectiveness research or what is now being called patient-centered outcomes research, and this is what this proposed legislation is against. Without research funded by agencies like AHRQ we’ll be flying blind when trying to advise patients about what works, doesn’t, and about potential harms.

**PG:** Of course.

**EB:** This kind of legislation does not appear to have any sort of rational basis or understanding of the way that the medicine is practiced or the way that people face health care decisions every day and you know, I would say that it is proposed legislation against patients.

### *In Brief*

## **Stand Up To Cancer Announces Celebrity Fundraising Telecast**

**STAND UPTO CANCER** will hold a fundraising telecast Sept. 7, with 100 percent of all public donations going directly to cancer research. ABC, CBS, FOX and NBC plan to donate one hour of simultaneous commercial-free airtime for the fundraising special, to be broadcast live from the Shrine Auditorium in Los Angeles.

HBO, HBO Latino, Bio, Lifetime Movie Network, Logo, MLB Network, mun2, Palladia and VH1 have also committed to carry the telecast. The program will include a celebrity phone and multi-media bank that will allow viewers to interact with those participating.

“This broadcast has become a global call-to-action for all those touched by cancer,” said Gwyneth Paltrow, co-executive producer of the telecast. “Like so many people, I know what it’s like to lose a family member to this disease, and I’m honored to stand up in my father’s memory.”

“Music and its ability to heal, unite and motivate will play a central role in this year’s show, as will the stories of people affected by cancer and how SU2C is changing their lives,” said co-executive producer Joel Gallen. “It’s an honor to build on the terrific legacy Laura Ziskin established with the previous two broadcasts.”

Film producer Laura Ziskin, who was a member of the SU2C Executive Leadership Council, executive produced the first two telecasts. Ziskin lived with breast cancer for seven years before she passed away in June of 2011.

The list of those participating in the telecast will be announced throughout the summer.

**THE AMERICAN ASSOCIATION FOR CANCER RESEARCH** announced a partnership with Kure It and called for nominations for the 2012 **AACR-Kure It Grant for Kidney Cancer Research**.

The two-year, \$250,000 grant will support a translational research project designed to improve the survival and quality of life of patients with kidney cancer and, in turn, lead to individualized therapeutic options for the treatment or development of promising new kidney cancer therapies.

The recipient will be recognized at the AACR’s 2013 annual meeting, April 6-10 in Washington, D.C.

Independent investigators are invited to submit proposals to develop and study new ideas and approaches that will have a direct application and relevance to patients with kidney cancer. The grant recipient will be selected by an expert scientific review committee of kidney cancer specialists assembled by the AACR.

The application deadline is 12:00 p.m. Eastern Time, Aug. 21.

**THE LEUKEMIA & LYMPHOMA SOCIETY Man & Woman of the Year** campaign raised \$18.9 million for blood cancer research and patient services. More than 800 candidates participated in the 10-week campaign, and the society surpassed last year’s fundraising record by \$4.2 million.

Leukemia survivor **Tommy Cleaver**, of Washington, D.C., and St. Louis-based jewelry

company owner **Mary Pillsbury Wainwright** emerged as the highest fundraisers, earning them the titles of national Man of the Year and Woman of the Year.

Cleaver, a 10-year survivor of chronic myelogenous leukemia and a vice president at CBRE, a commercial real estate services firm, raised \$271,933, the most ever raised by a candidate from the society's National Capital Area Chapter.

Pillsbury Wainwright single-handedly raised a total of \$259,333, the largest amount raised by a candidate representing the St. Louis Gateway Chapter.

### Drug Approvals

## **FDA Approves Kyprolis For Multiple Myeloma**

FDA approved **Kyprolis** to treat patients with multiple myeloma who have received at least two prior therapies.

The safety and effectiveness of Kyprolis (carfilzomib) was evaluated in a phase IIb study of 266 patients with relapsed multiple myeloma who had received at least two prior therapies, including Velcade (bortezomib) and Thalomid (thalidomide). Enrolled patients had received a median of five prior anti-myeloma regimens.

The study's primary efficacy endpoint was the rate of overall response, which was 22.9 percent. The median duration of response was 7.8 months. Currently, no data are available that demonstrate an improvement in progression-free survival or overall survival.

The most common side effects observed in more than 30 percent of the study participants were fatigue, low blood cell count and blood platelet levels, shortness of breath, diarrhea, and fever. Serious side effects included heart failure and shortness of breath.

The drug was approved under the accelerated approval program. Kyprolis is marketed by Onyx Pharmaceuticals.

FDA approved **Prepopik** for oral solution indicated for the cleansing of the colon as a preparation for colonoscopy in adults. Prepopik (sodium picosulfate, magnesium oxide, and anhydrous citric acid) is a low-volume, orange-flavored, dual-acting, stimulant and osmotic laxative.

Approval was based on two phase III non-inferiority studies in which Prepopik was compared to 2L PEG+E plus 2x 5-mg bisacodyl tablets. In both studies, Prepopik achieved the primary endpoint

(successful colon cleansing based on the Aronchick Scale), demonstrating non-inferiority to the comparator [Study 1: 84.2% v. 74.4%; Study 2: 83.0% v. 79.7%]. Additionally, Prepopik demonstrated statistical superiority in cleansing of the colon versus the comparator.

The most common adverse reactions were nausea, headache and vomiting. Once commercially available, Prepopik will be the lowest volume active ingredient colon preparation available—with 10 ounces of prep solution. Prepopik is sponsored by Ferring Pharmaceuticals Inc.

**The Committee for Medical Products for Human Use** of the European Medicines Agency recommended approval of **Dacogen** for Injection in the treatment of patients over the age of 65 with newly diagnosed de novo or secondary acute myeloid leukemia who are not candidates for standard induction chemotherapy.

The CHMP's positive opinion is now referred for approval to the European Commission. The drug's sponsor outside of North America, Janssen-Cilag International NV, anticipates receiving the regulatory decision from the Commission in the end of the third quarter of this year.

The opinion is based on data from the DACO-016 trial, the largest AML trial to date in this population of older patients. This randomized, open-label, multi-center phase III clinical trial compared Dacogen versus patient's choice with physician's advice of either supportive care or low-dose cytarabine in patients 65 years and older with newly diagnosed de novo or secondary acute myeloid leukemia and poor- or intermediate-risk cytogenetics.

Dacogen was administered at 20 mg/m<sup>2</sup> as a one-hour intravenous infusion once daily for five consecutive days, repeated every four weeks, continued as long as the patient derived benefit. Key results from this study were published in the Journal of Clinical Oncology in June 2012.

Dacogen is a DNA hypomethylating agent currently approved for the treatment of myelodysplastic syndromes in more than 30 countries, including the United States, Brazil, China, India, Korea, Russia and Turkey.

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