THE CANCER LETTER

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SPECIAL ISSUE

USPSTF To Downgrade PSA Screening From "I" to "D" — As In "Don't Do It"

By Paul Goldberg

Next week, the Obama administration will have to face another political explosion over cancer policy.

The U.S. Preventive Services Task Force plans to downgrade its recommendation of a procedure for screening prostate cancer, the prostate-specific antigen test, from its current grade—"I," for inconclusive—to "D," no benefit for screening men under the age of 75. Screening men over 75 already has a D recommendation.

The D rating means that "there is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits," according to the USPSTF website.

Insiders are wondering whether the administration will stand by another negative recommendation from the task force—or whether it will back down, as it did during the mammography debate of 2009.

For proponents of evidence-based medicine, the stakes in this controversy will be high. To them, the USPSTF is more than an obscure task force tucked into a corner of the Agency for Healthcare Research and Quality.

Rather, the task force is one of the most important products of the movement for evidence-based medicine, and—at least on paper—a pillar of evidence-based medicine within the U.S. government.

The purpose of the task force is to use a set of highly structured, pre-

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In Brief

FDA and NIH Announce National Tobacco Study; FDA Publishes Blueprint on Biomedical Innovation

FDA and **NIH** announced a national study to determine the behavioral and health impacts of new government tobacco regulations.

The **Tobacco Control Act National Longitudinal Study of Tobacco Users** is a joint research study that will monitor over 40,000 tobacco users as well as children over 12 who are at risk for tobacco use.

The objective is to identify what makes people susceptible to tobacco use, evaluate patterns and resulting health problems, study the patterns of tobacco cessation and relapse, evaluate the effects of regulatory changes on risk perceptions and other tobacco-related attitudes, and assess the differences in attitudes, behaviors, and key health outcomes in racial-ethnic, gender, and age subgroups.

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Delays In Taking a Vote Suggest Political Meddling with USPSTF

(Continued from page 1)

specified procedures to separate the science of screening from the politics of screening, and to safeguard the process from conflicts of interest.

The politics of today's PSA guideline and 2009's mammography guideline aren't identical.

The breast cancer guideline likely took the administration by surprise when it triggered a nationwide outcry during Congressional debates over the administration's healthcare reform proposal.

The task force recommended against routine mammography screening for women under the age of 50, and suggested that screening should be extended to every two years for women older than 50. Professional societies and patient advocacy organizations accused the Obama administration of attempting to ration healthcare.

But the making of the USPSTF prostate cancer guideline is anything but a surprise. Evidence indicates that politicians have been orchestrating the timing of the guideline's release for over two years, since November 2009.

The details of the timeframe emerged in a story that will appear in the next issue of The New York Times Magazine. The story was published online at http://www.nytimes.com/2011/10/09/magazine/can-cancer-ever-be-ignored.html?_r=1&ref=magazine

The story, by Shannon Brownlee and Jeanne Lenzer, broadly examines the prostate cancer screening controversy. A Q&A with Brownlee appears on page 5.

There are no indications of political interference with the content of the task force guideline on prostate cancer. However, the story includes a timeline that shows interference by forces outside HHS and apparent efforts to orchestrate the timing of release of the guideline.

In November 2009, the independent task force of experts first voted to downgrade PSA screening to a D rating, the NYT Magazine story reports.

Sources confirmed to The Cancer Letter that the task force had taken a vote several days prior to release of the breast cancer screening guidelines.

That recommendation caused a violent political firestorm, prompting HHS Secretary Kathleen Sebelius to distance herself from the task force and its recommendation (The Cancer Letter, Nov. 20, 2009).

For reasons that aren't publicly known, the prostate cancer recommendation was never formalized, sources said.

In November 2010, the task force was scheduled to vote again, the NYT Magazine story reports.

Ned Calonge, then the task force chair, sent the PSA recommendation back for review. The meeting was to occur before the mid-term elections. Calonge told the Times that word had leaked out that if the November meeting was held, it could jeopardize the task force's financing.

This is different from the explanation he gave to The Wall Street Journal at the time. He said the meeting was canceled because of scheduling conflicts. That story is posted at http://blogs.wsj.com/health/2010/10/26/prevention-task-force-cancels-nov-meeting-would-have-included-prostate-screening-vote/

Calonge eventually canceled the meeting, which deeply disappointed a staff member, Kenneth Lin, then a medical officer at AHRQ, who wrote about the aborted meeting in a blog post: http://commonsensemd.blogspot.com/2010/11/meeting-that-wasnt-and-surprise.html

Meanwhile, the administration had been involved in orchestrating the timing of actions of at least one other science-based agency, the FDA.

At the same time, just before the 2010 elections, FDA made a surprise announcement that it would delay its decision on withdrawing the accelerated approval of the drug Avastin for the metastatic breast cancer indication.

Though FDA cited submission of new data as the cause for the delay, breast cancer experts said that they were unaware of any new phase III data, and internal sources said that the delay was sought by the administration.

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Now it is up to the FDA Commissioner Margaret Hamburg to decide whether Avastin will keep its breast cancer indication.

Regarding the PSA screening test, the task force finally met in March 2011 and voted to lower the grade, and submitted a paper with comprehensive review of evidence to the Annals of Internal Medicine.

The Annals will publish a paper laying out the systematic review of evidence that accompanies the recommendation. The Cancer Letter obtained a late draft of the paper outside the embargo.

The recommendation approved by the committee will be posted on the USPSTF website late Tuesday, sources say.

The agency's original plan was to release the recommendation at a later date, but the timing was moved up because the NYT Magazine story sparked public interest in the matter, and at least two reporters had learned about the planned downgrade.

The agency's procedure for releasing recommendations has been changed as a result of the breast cancer screening debacle.

Now the agency releases "draft recommendations" and collects comment, in a procedure that vaguely mimics rulemaking. A contractor then organizes the comments and responds to them. This leaves the recommendation open to the possibility of changes.

The new procedure, in effect, can spread out the public's reaction over time, hold out the promise that changes would be made, and gives the agency the opportunity to back out of the guideline, saving face under the possibility of public pressure.

The Cancer Letter did not obtain the systematic review of evidence under an embargo, and therefore did not agree to uphold that embargo. As a matter of policy, we honor embargos even in situations when they don't directly apply to us. However, in the face of evidence of political orchestration of the timing of the announcement, we decided to make all information available to the public at the earliest possible time.

The entire USPSTF draft paper is posted at http://www.cancerletter.com/categories/documents.

The paper's abstract is posted below:

Background: Prostate specific antigen-based screening can detect prostate cancer in earlier, asymptomatic stages, when treatments might be more effective.

Purpose: To update the 2002 and 2008 U.S. Preventive Services Task Force evidence reviews on screening and treatments for prostate cancer.

Data Sources: MEDLINE (2002 to July 2011), the Cochrane Library Database (through the 2nd quarter of 2011) and reference lists.

Study Selection: Randomized trials of PSA-based screening; randomized trials and cohort studies of prostatectomy or radiation therapy versus watchful waiting for localized prostate cancer; and large (n>1000), uncontrolled observational studies of perioperative harms.

Data Extraction: Investigators abstracted details about the patient population, study design, data analysis, and results and assessed quality using predefined criteria.

Data Synthesis: Five randomized trials of screening and three randomized trials and 23 cohort studies of treatments met inclusion criteria. The two largest and highest-quality screening trials reported conflicting results. A European trial found screening associated with reduced prostate cancer mortality in a subgroup of men ages 55 to 69 years after 9 years (RR 0.80, 95% CI 0.65-0.98; absolute risk reduction 0.07%). A U.S. trial with high crossover and contamination rates found screening not associated with reduced prostate cancer mortality after 10 years. 12-13% of screened men had false-positive results after 3-4 screening rounds, and serious infections or urinary retention occurred after 0.5-1.0% of prostate biopsies. One good-quality randomized trial found prostatectomy for localized (primarily stage T2) prostate cancer associated with decreased risk of prostate cancer mortality compared to watchful waiting through 13 years follow-up (RR 0.62, 95% CI 0.44-0.87; absolute risk reduction 6.1%); subgroup analyses suggested benefits were limited to men <65 years of age. Treating approximately three men with prostatectomy or seven men with radiation therapy instead of watchful waiting would each result in one additional case of erectile dysfunction, and treating approximately five men with prostatectomy would result in one additional case of urinary incontinence. Prostatectomy was also associated with perioperative (30-day) mortality (about 0.5%) and cardiovascular events (0.6% to 3%) and radiation therapy with an increased risk of bowel dysfunction.

Limitations: Only English language articles were included, few randomized treatment trials met inclusion criteria, and few studies evaluated newer therapies.

Conclusions: After about 10 years, PSA-based screening results in small or no reduction in prostate cancer-specific mortality and is associated with harms related to subsequent evaluation and treatments, some of which may be unnecessary.

Primary Funding Source: Agency for Healthcare

Research and Quality

Prostate cancer is the most commonly diagnosed cancer in American men [1-3]. Prostate-specific antigen (PSA)-based screening can detect prostate cancers in earlier, asymptomatic stages, when treatments might be more effective.

The U.S. Preventive Services Task Force (USPSTF) last reviewed the evidence on prostate cancer screening and issued recommendations in 2008. Since then, large trials of prostate cancer screening have been published. Benefits and harms of treatments for prostate cancer were last reviewed by the USPSTF in 2002. This article summarizes two reviews commissioned by the USPSTF to synthesize the current evidence on screening and treatments for localized prostate cancer, addressing the following Key Questions:

Key Questions:

1. Does PSA-based screening decrease prostate cancer-specific or all-cause mortality?

2. What are the harms of PSA-based screening for prostate cancer?

3. What are the benefits of treatment of early-stage or screen-detected prostate cancer?

4. What are the harms of treatment of early-stage or screen-detected prostate cancer?

PSA Screening

Brownlee: Task Force Independence Is At Stake In Debate Over PSA

The Cancer Letter invited Shannon Brownlee, a co-author of the New York Times Magazine story about prostate cancer screening, to discuss her finding that the timing of release of the U.S. Preventive Services Task Force recommendation may have been influenced by political considerations.

Brownlee is acting director of the New America Foundation Health Policy Program and an instructor at Dartmouth Institute for Health Policy and Clinical Practice. Her co-author, Jeanne Lenzer is a freelance journalist.

The story is posted at http://www.nytimes.com/2011/10/09/magazine/can-cancer-ever-be-ignored.html?_r=1&ref=magazine

The interview was conducted by Paul Goldberg, editor and publisher of The Cancer Letter.

PG: First of all, congratulations. To me, the most fascinating part of the story was your account of the delays in the task force votes. This is huge.

SB: You mean the findings of what the evidence says about PSA testing is huge?

PG: Right. No, what I'm talking about is that the task force didn't just sit down, vote, and move on. Instead, there were these near-votes, aborted meetings. Do you see political interference or orchestration of the timing?

SB: I don't know so much if it's political orchestration as it's fear that's part of the timing. Remember the ferocious reaction to the US Preventive Services Task Force recommendations on mammography? I don't know if they were caught unawares, but they certainly got slammed hard for it. And so you have to sort of wonder whether or not their effort to provide guidance was completely mitigated by the reaction that they got.

PG: I guess what I've never seen before is evidence that there would be a vote, and then the vote is forgotten. What happened when the committee voted in 2009? Nobody knows. And then there's another vote and the task force meeting is canceled. This is political orchestration of some sort, isn't it?

SB: Yeah we're looking into it, let's put it this way. We can certainly say that the task force felt political pressure in the form of worrying about losing funding if they came out with the PSA recommendation. I don't know whether or not coming out now is going to make a difference to Congress versus coming out back then, right before the election in 2010.

PG: I guess the question I'm asking is, Do you think the public realizes that this is not just a little agency tucked in the corner of HHS. And this is actually an agency that's created in order to separate the politics of screening from the science of screening—and therefore hands-off?

SB: It's supposed to work that way. That's the point of having an independent task force—to separate the politics from the science. And the tragedy here looks like it got mixed up, despite efforts to keep them apart.

PG: That's why your story is so incredible, so unbelievable. Let me paraphrase, it's credible, it's believable, and it's scary.

SB: It is scary. That's the reason we have a task force. To come out with recommendations that are not politically motivated, they're not motivated by cost concerns, but that are based in good science.

PG: So why the AHRQ if you're going to be politically playing with it? Why have a task force when you're going to be playing with it politically.

SB: That's a good question. I think we need the task force desperately. Now more than ever.

PG: This evidence-based medicine versus politics?

SB: Versus faith-based medicine. I think that's exactly right. This is whether or not the task force will be permitted to do its job independently is really a crucial test of whether or not we're ready to use science in the way that it should be used.

PG: My checking shows that you are absolutely on target with your time frame of the votes. Was this an effort to find the optimal time to release a finding that will be political explosive?

SB: There is no optimal time.

PG: That was my question.

SB: That's a cruel joke. There is no optimal time. This is going to be met with dismay, and fear and loathing no matter when they release it. It is not going to be palatable to the patient advocacy community—much of the patient advocacy community, I should say. There are patient advocates out there that are science based, that are reasonable, that understand the difficulties of these scientific questions and are willing to listen to what the science says. But a lot of the advocacy community is going to react to this explosively no matter when they release it.

PG: So what's the take home?

SB: I think the take home is that we have to make sure that the U.S. Preventive Services Task Force is better insulated. I mean maybe the take home for the task force is learning how to release information.

PG: There was a change in the procedure that AHRQ is using to release the task force recommendations now. Have you looked at that?

SB: I have no idea. I didn't know there was.

PG: What they are doing now is they are going to publish on Tuesday night or Wednesday morning. They will put it on their website, no press release, just a little note saying that the draft recommendation has been issued. There's going to be a month of public comment. Why is public comment necessary if the whole purpose of the task force is to rely on pre-specification of procedures?

SB: I don't know. It's like public comment—oh great. So this is science by consensus? This is science by mob rule? That's crazy.

PG: If we are going to do this, why have task force, why have science?

SB: Why have a preventive services task force that you've given this job of doing a careful review of what the evidence says. Why bother? Why not just put a recommendation out there and do crowd-sourcing on it?

In Brief:

FDA Publishes Blueprint On Driving Biomedical Innovation

(Continued from page 1)

"The launch of this study signals a major milestone in addressing one of the most significant public health burdens of the 21st century," said FDA Commissioner Margaret Hamburg. "The results will strengthen FDA's ability to fulfill our mission to make tobacco-related death and disease part of America's past and will further guide us in targeting the most effective actions to decrease the huge toll of tobacco use on our nation's health."

FDA released a blueprint containing immediate steps that can be taken to drive biomedical innovation.

The blueprint, **Driving Biomedical Innovation: Initiatives for Improving Products for Patients,** addresses concerns about the sustainability of the medical product development pipeline.

It includes steps such as: rebuilding FDA's small business outreach services, building infrastructure to drive and support personalized medicine, creating a rapid drug development pathway for important targeted therapies, harnessing the potential of data mining and information sharing while protecting patient privacy, improving consistency and clarity in the medical device review process, training the next generation of innovators, and streamlining and reforming FDA regulations.

The **NATIONAL ORGANIZATION for RARE DISORDERS** is requesting more input on decisions related to relative risk and potential benefit for new drugs and medical devices from the FDA.

They requests are for enhanced communication between the patient community and FDA to ensure that the voices of patients with chronic and rare diseases are

heard in risk-benefit determinations and related policy decisions.

"Patients need to have opportunities to communicate with FDA medical reviewers on the risks they are willing to run in exchange for a potential though unproven benefit," said Peter Saltonstall, president and CEO of NORD. "For example, a patient with a serious disease and no approved therapy may have a perception of risk that is very different from that of someone who has treatment alternatives. We believe that FDA can make more informed decisions about investigational products and about which products to approve if they hear directly from patients."

THE ASSOCIATION of COMMUNITY CANCER CENTERS announced the winners of the first annual **ACCC Innovator Awards**, to honor members that have exhibited forward-thinking strategic planning and developed pioneering programs. They will be recognized at the National Oncology Conference in Seattle on Oct. 21.

Fourteen cancer programs were selected. They are: Aurora St. Luke's Medical Center Cancer Center; Bridgeport Hospital's Norma F. Pfriem Cancer Institute; Kansas City Cancer Center; Memorial University Medical Center, Curtis and Elizabeth Anderson Cancer Institute; Mountain States Tumor Institute, St. Luke's Regional Medical Center; MultiCare Health System, Multicare Regional Cancer Center; collaboratively Nancy N. and J.C Lewis Cancer & Research Pavilion at St. Joseph's/Candler, Harbin Clinic, The Medical Center Inc., and John B. Amos Cancer Center; Oregon Health and Science University, Knight Cancer Institute; Southside Regional Medical Center Cancer Center; Spartanburg Regional Medical Center, Marsha & Jimmy Gibbs Regional Cancer Center; and University of Colorado Hospital UC Cancer Center.

"These community cancer centers are quite diverse—representing all regions of the country, programs of all sizes, and with varying levels of resources." said ACCC President Thomas Whittaker. "They share, however, the will, the drive, and the spirit to leverage technology, improve planning and management processes, and empower their staff and their patients."

THE CANCER INSTITUTE OF NEW JERSEY is expanding research efforts as part of a new consortium of four studies in African-American women to examine the causes behind why African-American women are more likely to be diagnosed with breast cancer younger and at a later stage.

The Women's Circle of Health Study, the Carolina Breast Cancer Study, the Black Women's Health Study, and the Multiethnic Cohort Study will examine 11,000 women—half of which have breast cancer and have of which do not—in the largest ever study of it's kind. The NCI has awarded $19.3 million to the effort which is led by Christine Ambrosone, of Roswell Park Cancer Institute, Julie Palmer, of Boston University, and Robert Millikan of the Universtiy of North Carolina at Chapel Hill.

THE WISTAR INSTITUTE has broken ground on a seven-story, 89,700 square-foot research center that will expand Wistar's research operations.

"At a time when biomedical research is advancing at a lightning pace, The Wistar Institute finds itself constrained by aging facilities designed for 19th and 20th century science," said Wistar President and CEO Russel Kaufman. "We designed our new building specifically to foster interactions between researchers in the kinds of multidisciplinary collaborations that spark innovation and drive results."

THE COMMISSION OF CANCER of the **American College of Surgeons** has introduced a new data collection network to promote and facilitate evidence-based cancer care.

The **Rapid Quality Reporting System** has been introduced to over 1,500 hospital cancer programs. The RQRS was developed to assess how well CoC-accredited cancer programs adhere to specific cancer care recommendations when caring for patients with breast, colon, or rectal cancer. RQRS is a voluntary web-based data RQRS is believed to be the first national system for any disease that tracks care over time.

"A key issue in cancer care is that people require treatment over a period of time, often administered by a number of different doctors in different specialties, such as surgeons, radiation oncologists, and medical oncologists," said Stephen Edge, chair of the Commission on Cancer.

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The University of California, Irvine is recruiting for a basic, clinical and/or translational scientist. This position will be at the level of full professor 1.0 FTE (tenured), who will enter as the Deputy Director of the Cancer Center, with subsequent anticipated advancement to the position of Cancer Center Director. This is a senior leadership position within a National Cancer Institute designated Comprehensive Cancer Center.

The current long-term and highly successful Director has announced his departure from this role following the next Cancer Center Support Grant (CCSG) review scheduled for 2013; thus the timeline for transition to Directorship is firmly established. Applicants must hold an MD or equivalent degree. The ideal candidate will be an experienced physician scientist with a strong track record of NIH/NCI-funded research and a proven track record in senior leadership in NCI-designated cancer centers. Responsibilities of the selected individual would include:

1. Providing senior leadership for UC Irvine NCI-designated Comprehensive Cancer Center.
2. Managing the research infrastructure within the Cancer Center.
3. Facilitating the establishment and conduct of translational research programs with external peer-reviewed funding.
4. Bridging basic, clinical and cancer control research among the multiple research programs with the goal of facilitating translational programs, P01s, SPOREs and other multi-investigator grants.
5. Representing the Cancer Center throughout the campus and greater community.

In addition to the UC Irvine School of Medicine and the UC Irvine Medical Center, the Chao Family Comprehensive Cancer Center conducts research involving multiple schools within the University of California at Irvine. Of note, UC Irvine is home to a recently awarded NIH Clinical Translational Science Award, the Sue and Bill Gross Stem Cell Research Center, a CIRM Institute opened in 2010, the Institute for Immunology, the new Center for Epigenetics and Metabolism, the Health Policy Research Institute and the recently constructed UC Irvine Douglas University Hospital, one of the most technologically advanced hospitals in southern California and recognized by *US News & World Report* as among the best hospitals for oncology treatment.

TO APPLY: Please log onto UC Irvine's RECRUIT located at https://recruit.ap.uci.edu/apply. Applicants should complete an online application profile and upload the following application materials electronically to be considered for this position:

1. Letter of Interest **2.** Curriculum vitae including record of research experience **3.** 4-page NIH-formatted biosketch **4.** Names of at least three referees

The University of California, Irvine is an equal opportunity employer committed to excellence through diversity and strongly encourages applications from all qualified applicants including women and minorities. UCI is the recipient of a National Science Foundation ADVANCE award for gender equity.