Final USPSTF Guidelines: No to Routine PSA Testing

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May 21, 2012 — It's final. The US Preventive Services Task Force (USPSTF) now officially recommends against routine prostate-specific antigen (PSA)–based prostate cancer screening for healthy men, regardless of age.

Today the Task Force released its final recommendations for the screening after a period for public comment on a draft of the report. The new document is published online May 22 in *Annals of Internal Medicine*.

"The USPSTF concludes that there is moderate certainty that the benefits of PSA-based screening for prostate cancer do not outweigh the harms," reads the final assessment.

The USPSTF last published recommendations on prostate cancer screening in 2008. At that time, researchers concluded that there was no evidence to support PSA testing for men older than age 75.

Now this recommendation extends to all men. The Task Force has given the screening a "D" rating, which means "there is moderate or high certainty that the service has no benefit or that the harms outweigh the benefits."

The USPSTF's rating and its simplicity galled a prominent American urologist.

"Their formula requires that it [screening] be distilled into a sound byte, a sound letter: D," said Ian Thompson, MD, from the University of Texas Health Science Center at San Antonio and an American Urological Association (AUA) spokesperson. He discussed the recommendations with *Medscape Medical News*.

For men under the age of 75, the USPSTF previously graded the screening as an "I," which means there is insufficient evidence to assess the balance of benefits and harms.

"The D rating says 'Don't do it. Don't even have a discussion with the patient,' " said Dr. Thompson about the impression the rating creates. However, he acknowledged that the Task Force does recommend that clinicians discuss potential of testing with specific individual patients.

"Clinicians should understand the evidence but individualize decision making to the specific patient or situation," states the new document, the lead author of which is Virginia Moyer, MD, MPH, from Baylor College of Medicine in Houston, Texas.

But that recommendation to individualize discussion is "buried" in the document, said Dr. Thompson. "It's a disservice to the US public."

[It is] inappropriate and irresponsible to issue a blanket statement against PSA testing.

In a statement, the AUA blasted the USPSTF's D rating, saying that it is "inappropriate and irresponsible to issue a blanket statement against PSA testing."

"Men who are in good health and have more than a 10-15 year life expectancy should have the choice to be tested and not discouraged from doing so," according to the AUA.

Urologists attending the annual meeting of the AUA evidently do not agree with the new recommendations. At a town hall meeting at the conference today, a speaker asked the assembled attendees if they

disagreed with the USPSTF. Almost everyone in the ballroom raised their hands, reports a Medscape staff member in attendance. Only a few indicated that they agreed.

Individualized Decision-Making

Individualized decision-making is the route clinicians should take with patients, according to a published editorial that accompanies the new USPSTF report.

"We suggest that physicians…individualize prostate cancer screening decisions on the basis of informed patient preferences," write the editorialists, who are a group of high-profile urologists led by William Catalona, MD, from Northwestern University Feinberg School of Medicine, Chicago, Illinois, and Patrick Walsh, MD, from James Buchanan Brady Urologic Institute at Johns Hopkins Medical Institutions, Baltimore, Maryland.

Informed decision-making that acknowledges the harms of PSA screening is also recommended by the American Cancer Society (ACS), writes Otis Brawley, MD, in an essay that accompanies the new recommendations and the editorial by the team of urologists. He is the chief medical officer of the ACS.

Dr. Brawley says that other organizations, such as the European Association of Urology and the National Comprehensive Cancer Network, also recommend informed decision-making that examines harms and benefits.

However, Dr. Brawley is not a great believer in the benefit of PSA-based prostate cancer screening, as demonstrated to date. "The harms are well-proven, whereas the evidence of benefit is weak," he concludes, echoing the conclusions of the USPSTF report.

The evidence of benefit is weak.

He also acknowledged the "shock" that many Americans felt when they first heard about the USPSTF's draft recommendation because early detection of cancer through screening has been synonymous with improved survival in the minds of many Americans.

However, not all Americans were shocked. When the draft recommendation was first published as a draft report in 2011, the scientist who discovered the original PSA, Richard Ablin, PhD, from the University of Arizona College of Medicine in Tucson, told *Medscape Medical News* that he was "elated."

Dr. Ablin has long argued that the PSA test should not be used for routine screening of healthy men because it is not specific for prostate cancer. He also famously described the testing as a "public health disaster."

The earlier draft report also resulted in a multitude of writings and commentary, some of which reminded readers of basic issues.

The USPSTF statement is "a recommendation, not an edict," wrote Harvey Simon, MD, associate professor of medicine at Harvard and editor-in-chief of *Harvard Men's Health Watch*.

Dr. Simon noted that the recommendation reflects research studies published over the past few years that have questioned the benefit of screening and, as such, "the USPSTF statement really is an evolutionary development, not a revolutionary change."

The debate is ongoing, and "we are still a long way from concluding the discussion," he said.

The Evidence and Its Controversies

The pivotal data that led the USPSTF to downgrade its assessment of PSA-based prostate cancer screening from an I in 2008 to a D in 2012 come from 2 highly publicized screening trials.

The US PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial and the ERSPC (European Randomized Study of Screening for Prostate Cancer) were the "principal trials considered by the USPSTF," say the authors.

"The U.S. trial did not demonstrate any prostate cancer mortality reduction," they summarize.

"The European trial found a reduction in prostate cancer deaths of approximately 1 death per 1000 men screened in a subgroup of men aged 55 to 69 years. This result was heavily influenced by the results of 2 countries; 5 of the 7 countries reporting results did not find a statistically significant reduction," they also report.

But Dr. Catalona and his co-editorialists issue a big challenge to the USPSTF: They say that PLCO is not really a screening trial.

A host of issues "impair the claim that the PLCO is a true screening trial," they write.

The biggest issue with PLCO is that the control group in the study was "contaminated," they say. More than 50% of the controls, who were supposed to receive no PSA testing, did in fact have a PSA test during the first 6 years of the study. Earlier this year, an investigator of PLCO, which has been widely reported as showing that screening had no benefit, said "maybe there is a benefit" in an interview with *Medscape Medical News*. The admission was an accommodation of the fact of this widespread PSA screening in the study control group.

PLCO "didn't have a pure control group," admitted Philip Prorok, PhD, from the National Institutes of Health in Bethesda, Maryland, earlier this year when a study update was published. But he and his coauthors also had previously said any benefit that might have been found in the screening group of the study would have been "modest." In other words, if there was a benefit it was small.

Nevertheless, the USPSTF suggested that the PLCO provides valuable data because of its American-ness. "The screening intervals, PSA thresholds, use of digital rectal examinations, enrollee characteristics, and follow-up diagnostic and treatment strategies used in the PLCO trial are most applicable to current U.S. settings and practice patterns," the authors write.

Dr. Thompson said that the ERSPC is by far the stronger evidence.

The ESPRC found a significant decrease in the rate of prostate cancer mortality between the screening and control groups (rate ratio, 0.80; 95% CI, 0.65 - 0.98; *P* = .04), or a relative reduction of 20% in the rate of death from prostate cancer.

But the benefit in prostate cancer mortality after 10 to 14 years from the screening is "at most, very small" says the USPSTF report, "even for men in what seems to be the optimal age range of 55 to 69 years."

And while the benefit is small, the harms are "at least moderate" according to the USPSTF.

Nearly 90% of men with PSA-detected prostate cancer undergo early treatment with surgery, radiation, or androgen deprivation therapy. "Adequate evidence shows that up to 5 in 1000 men will die within 1 month of prostate cancer surgery and between 10 and 70 men will have serious complications," says the USPSTF.

When all the evidence was evaluated, the harms are greater than the benefits, concluded the USPSTF.

Dr. Thompson suggested it was anyone's guess as to how the recommendations would influence behavior. But he worried PSA testing will decline.

"My fear is it will take us back to the bad old days," he said, referring to prescreening era in which a higher proportion of advanced cancers were seen than are seen today.

The USPSTF members have disclosed no relevant financial relationships. Dr. Thompson and Dr. Brawley have disclosed no relevant financial relationships. Among various other conflicts of interest, Dr. Catalona is a consultant to Beckman Coulter Inc, which manufacturers PSA assays, and to OHMX Inc, which has a urine-based PSA activity assay in development of which he is co-inventor.

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