By Renee Twombly

For years, physicians and their patients have decided, on an individual basis, whether or not to use a prostate-specific antigen (PSA) screening test, which can detect not only life-threatening prostate cancer but also many cancers that may never pose a danger. No clear evidence exists for whether the test provides more benefit or harm, given the aggressive treatments that often follow a positive cancer diagnosis, and so patients and physicians face a difficult choice about whether to use the test.

Without definitive data, the U.S. Preventive Services Task Force (USPSTF), part of the federal Agency for Healthcare Research and Quality, issued guidelines in 1996 and again in 2002 that said it cannot recommend for or against PSA testing. Many other organizations that provide guidance to physicians ordering PSA tests—such as the American Cancer Society, the American College of Physicians, and the American Academy of Family Physicians (AAFP)—also adopted this position.

Despite the lack of evidence, the PSA test became popular, especially for older men. In 2006, more than 58% of men aged 50–59 years had a PSA test within the past 2 years, according to prevalence data compiled by the U.S. Centers for Disease Control and Prevention. Older men used the test much more often. The Centers for Disease Control and Prevention reported that 72% of men aged 60–64 years had a PSA test, and for men aged 65 years and older, it was almost 77%.

PSA testing has also led to unprecedented rates of treatment for prostate cancer: More than 90% of men diagnosed with the disease receive some form of treatment, even though many researchers believe that most prostate cancer cases will never become a health issue. Only about one-sixth of patients diagnosed with prostate cancer ultimately succumb to the disease, but there is no way currently to identify which prostate cancers should be treated aggressively.

Now, citing new findings, the USPSTF has recommended that men aged 75 years and older not be screened with the PSA test, and it reiterates that the benefits of the test are still unproven in younger ages.

The USPSTF laid out its recommendations in the August 5 issue of the Annals of Internal Medicine, saying that men who have a life expectancy of 10 or fewer years would suffer more immediate harm than long-term benefit from the consequences of a PSA screening test. U.S. population figures show that most men don’t live beyond age 85. About 71% of deaths from prostate cancer occurred in men older than 75 years. And because dying from prostate cancer once it is diagnosed often takes at least a decade, men this age will probably die from other causes before the cancer kills them. Therefore, task force members say age 75 years should be the cutoff for prostate cancer screening.

But some physicians predict that the USPSTF’s revised guideline will generally be ignored—particularly by urologists—for a variety of reasons, including fears of age discrimination, ingrained medical practice, and health care economics.

The new guidelines are “understandable and reasonable” when one considers that there are no randomized clinical trials that have yet demonstrated a mortality benefit to men who were screened with PSA or digital rectal exams at any age, said Peter Scardino, M.D., chairman of the department of surgery at Memorial Sloan-Kettering Cancer Center. “From a public health point of view, screening has not been proven. But what makes sense in theory may not in practice,” Scardino said.

“If an older man comes in and says he wants a PSA test, I think any doctor will agree to it.”

“The USPSTF guidelines, for the most part, have been received with indifference by the medical community, in my opinion,” said David Penson, M.D., a urologist at the University of Southern California.

Establishing an age-specific cutoff time is “arbitrary and unfair and might deny men a potentially beneficial intervention,” he said.

In any case, “the proverbial cat is out of the bag,” Penson said. “One of the biggest issues that clinicians face is that patients demand prostate cancer screening, regardless of their age. It is difficult to convince patients otherwise, even if it is absolutely clear that they will not benefit from screening.”

Different Viewpoints, Limited Data

Physicians who believe in the value of PSA screening point out that the mortality rate for prostate cancer has been declining in the United States in the last
two decades, which suggests to some that PSA and digital rectal exams are finding prostate cancers early enough to save lives.

Data from the U.S. cancer registries, including the SEER (the Surveillance, Epidemiology, and End Results [SEER]) database, show that “during the PSA era, the percentage of prostate cancer cases that have metastases at the time of diagnosis has decreased by 75%, and PSA testing has produced an unprecedented stage shift—more than for any other tumor,” said William Catalona, M.D., professor of urology at Northwestern University. The relative 5-year survival rate for prostate cancer has increased from about 75% to about 99%, and there has been a corresponding 35% reduction in the age-adjusted prostate mortality rate in the U.S. from use of PSA, said Catalona, who helped develop the PSA test. “There are also recent studies estimating that between 40% and 70% of the reduction of prostate cancer–specific deaths is due to PSA testing.”

But public health experts say that Catalona’s use of statistics and observations don’t prove the benefits of prostate cancer screening and that the issue will not be answered until results are available from two ongoing randomized screening trials: the U.S. Prostate, Lung, Colorectal, and Ovarian (PLCO) Screening trial and the European Study of Screening for Prostate Cancer.

When the USPSTF reexamined its prostate cancer screening guidelines during a mandatory 5-year review, the previous conclusions still held, in general: USPSTF cannot recommend for or against prostate cancer screening for any man, and men who had a life expectancy of fewer than 10 years should not be screened.

However, they also considered new evidence that led to the age cutoff, according to Ned Calonge, M.D., chair of USPSTF. Although most PSA screening studies from 2002 to 2007 that the task force considered were of poor quality, he said, one study in particular was relevant—the Scandinavian Prostate Cancer Group Study No. 4, which was published May 12, 2005, in the New England Journal of Medicine. In this clinical trial, men diagnosed with early prostate cancer were randomly assigned to either radical prostatectomy (347 patients) or to watchful waiting (348 men). Investigators found a small absolute reduction in the risk of death after 10 years among those who were treated, but reductions in the risks of metastasis and local tumor progression. Treated patients (all ages included) had a relative reduction of 40% in the risks of distant metastasis and 67% in local progression, compared with untreated men.

A subanalysis of older men caught the attention of the task force, said Calonge, who is also chief medical officer of the Colorado Department of Public Health and Environment. As reported in the New England Journal of Medicine, after a median of 10.8 years there was no discernible difference in prostate cancer–specific deaths due to PSA testing.

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Calonge agrees, saying that although the Scandinavian study was not a screening trial, it did chart the natural history of men diagnosed with prostate cancer who were not treated. “It showed us that you needed to live longer than 10 years if you hope to benefit from early detection through screening, and from that we took a conservative message, saying men over 75 should not be screened because most 75-year-olds are not going to live another decade.”

With the side effects from many prostate cancer treatments, including reduction in quality of life, there is a tipping point at which harm outweighs benefit, and “we firmly believe that men 75 and older are being harmed every day with the consequences of the PSA test,” Calonge said.

Some physicians argue that an age cutoff is arbitrary and perhaps discriminatory and that many men have long life expectancies. “It’s very difficult with our aging population, and with the patients that we’ve been seeing now for years that have been screened since around 1988. It’s very difficult for us to just say at 75, we’re no longer going to provide screening for those patients,” said J. Brantley Thrasher, M.D., a spokesman for the American Urological Association and the American Urological Association Foundation. “Some have been screened for years and come in requesting PSA. Others come in and are very healthy at 75 [and] have at least 10 years of life expectancy,” said Thrasher, who is also chair of the department of urology at the University of Kansas Medical Center.

Calonge does not agree that establishing an age cutoff date for PSA testing is arbitrary. “I have to take issue with the point that anyone actually can say how much longer a 75-year-old man is going to live,” says Calonge. Even if a man lives to 90, treating his prostate cancer after age 75 “is not going to buy him any health outcome for at least 10 years. The Scandinavian
study says there is no difference in whether you treat them or not.”

“Temper the Guideline as Needed”

Colin Dinney, M.D., chairman of the department of urology at the University of Texas M. D. Anderson Cancer Center, said that he has long been convinced that older men do not benefit from PSA screening. His institution has not been offering PSA screening to men aged 75 years or older for the past 10 years. “If you don’t limit the screening, you run the risk of overdiagnosing cancers that aren’t biologically significant, and that is especially true in older men, who are much more likely to have higher PSA scores,” he said.

Dinney also says that the math doesn’t make sense. “On average, it takes 10–15 years or more to succumb to the disease once diagnosed, and half of patients who die of prostate cancer will have died by age 80, so why do the test in these older men?”

Still, that’s not to say that doctors would turn down a request for a PSA test from a healthy elderly man. “You have to temper the guideline as needed,” Dinney said.

“I believe we are overtreating prostate cancer in men in this age group, but I also doubt it will change any urologist’s practice because the profession as a whole is convinced that PSA screening is beneficial,” said John Hopkins’ Carter. He believes that PSA screening will continue in men of all ages because of several factors: “Number one is a patient’s and a physician’s fear of missing the window of opportunity for a cure,” he said, and the second reason is an associated fear of litigation. “I think physicians are oftentimes worried about telling a person with cancer that it probably won’t harm him,” Carter said.

Another important reason is that there are economic motivations to offer the test, when one considers the treatments that follow, he said. “And that is true both on the part of physicians and hospitals,” Carter said. For example, because robotic radical prostatectomy has become so popular, “robot mills” are on the rise, he said. In fact, Hopkins is buying several more robots for its clinic, Carter said, but he added that the institution also has the largest surveillance program in the world—more than 600 men are enrolled in a “watchful waiting” study. “I believe we are overtreating prostate cancer and that there is more harm than benefit in men 75 and older—but I also believe that early detection with PSA screening saves lives and that there are men over age 75 who might benefit from a PSA test,” Carter said.

General internists and family doctors “have long had a suspicion that PSA screening causes more harm than good in men older than 75,” said Doug Campos-Outcalt, M.D., who serves as the AAFP’s staff liaison to the prevention task force. The new guidelines, which Campos-Outcalt believes that the AAFP will adopt, will “provide a little more ammunition” for physicians not to offer the test to their elderly patients. “A lot of older men are getting the test now and don’t know it. PSA is done so widely that it is a part of a routine screening panel,” said Campos-Outcalt, who is also associate chair of the department of family and community medicine at the University of Arizona College of Medicine.

Still, even though there is not a financial incentive for them to offer the test, “family physicians are pretty independently minded, as are patients, and they will make their own decisions,” Campos-Outcalt said. “No one will turn a patient down if he really wants the test.”

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