Prostate Cancer Screening Reduces Deaths, but Controversy Remains

A new analysis of past studies shows that PSA screening reduces mortality but may lead to unnecessary treatment.

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Should all men be screened for prostate cancer? Despite a large and growing body of evidence, this remains a vexing question. New research continues to shed more light on the benefits and risks of routine prostate-specific antigen (PSA) screening, but experts continue to disagree about how the pluses and minuses balance out.

PSA screening can detect aggressive prostate cancer, allowing for earlier and more effective treatment. But routine testing can also diagnose slow-growing cancer in men who will likely die of other causes, and unnecessary treatment can lead to reduced quality of life. In April, an expert task force recommended that men should discuss the potential benefits and harms of screening with their provider and make decisions guided by their personal preferences.

Cancer of the prostate, a gland near the bladder that produces seminal fluid, is one of the most common cancers among men in the United States and the third-leading cause of cancer death among men, according to the American Cancer Society.

Prostate cancer typically grows slowly. It usually does not cause symptoms in its early stages—and often never does. A majority of men diagnosed with this type of cancer are over age 65, and most will not die from it. While an estimated one in seven men will be diagnosed with prostate cancer in their lifetime, only one in 39 will die from it.

Prostate cancer can be detected by a blood test that measures prostate-specific antigen, a protein produced by the gland. But PSA tests don’t tell how aggressive or advanced the cancer is or whether it will respond to treatment. Digital rectal exams are also used to detect abnormal prostate enlargement or lumps.

Men with positive PSA tests face a decision between “watchful waiting” to see whether the cancer progresses or treatment with some combination of surgery, radiation and chemotherapy, which can lead to adverse outcomes, including urinary incontinence and impaired sexual function.

Routine screening—testing all men within a certain age range regardless of whether they have
symptoms—will catch some aggressive cancers that otherwise would have gone untreated. But it will also detect slow-growing cancers, leading some men to undergo treatment they don’t really need.

Current Recommendations

New research and shifting expert opinions about the balance of benefits and harms has led to changes in recommendations about which men should receive prostate cancer screening and when.

The PSA test was developed in the 1980s, and in 1994, the Food and Drug Administration approved it as a screening tool for prostate cancer. In 2002, the U.S. Preventive Services Task Force (USPSTF) said there was not enough evidence to recommend either for or against routine PSA screening or digital rectal exams. In 2008, based on a review of more recent research, the task force recommended against prostate cancer screening for men age 75 and older but concluded that the evidence was “insufficient to assess the balance of benefits and harms” for younger men. In 2012, the task force went further, recommending against PSA screening for men in the general population regardless of age.

But this past April, the USPSTF walked back its stance against routine prostate cancer screening. The latest draft (which has gone through a public comment period but has not yet been finalized) recommends against PSA screening for men age 70 and older. But for men between the ages of 55 and 69, the task force offers more leeway for individualized decisions.

“Screening offers a small potential benefit of reducing the chance of dying of prostate cancer. However, many men will experience potential harms of screening, including false-positive results that require additional workup, overdiagnosis and overtreatment, and treatment complications such as incontinence and impotence,” the draft states. “The USPSTF recommends individualized decision making about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision.”

Similarly, the American College of Physicians (ACP) advises that although the chances of harm from PSA testing will outweigh the benefits for most men, clinicians and patients between the ages of 50 and 69 should discuss the benefits and harms of screening, the patient’s general health and life expectancy and patient preferences. The ACP recommends against screening for men younger than 50 or older than 69.

The American Urological Association (AUA) recommends against PSA screening for men younger than 40 and does not recommend it for men ages 40 to 54 at average risk. But the AUA acknowledges that some men under age 55—such as African-American men and those with a family history of cancer—are at higher risk and that screening should be individualized. For men ages 55 to 69, “the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in 1 man for every 1,000 men screened over a decade
against the known potential harms associated with screening and treatment.” The AUA experts suggest that screening every two years rather than annually is likely to “preserve the majority of the benefits and reduce overdiagnosis and false positives.”

The American Cancer Society recommends that starting at age 50 men should talk to a provider about the pros and cons of testing so they can decide whether testing is the right choice for them. Those who are African American or who have a father or brother who had prostate cancer before age 65 should have this talk starting at age 45. “We believe that men should not be tested without first learning about what we know and don’t know about the risks and possible benefits of testing and treatment,” the ACS states.

These recommendations encourage men to take an active role in their health care by learning about the latest research on the benefits and risks of prostate cancer screening.

More Evidence of Benefit

One such study, recently published in the Annals of Internal Medicine, took an in-depth look at two large studies of prostate cancer screening that came to different conclusions. One showed that screening decreased prostate cancer mortality; the other showed no reduction. Current guidelines rely heavily on the conflicting findings from these studies.

Ruth Etzioni, PhD, of Fred Hutchinson Cancer Research Center in Seattle and her colleagues analyzed data from the European Randomized Study of Screening for Prostate Cancer (ERSPC), which enrolled around 162,000 men ages 55 to 69 in several European countries, and the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO), which included more than 76,000 men ages 55 to 74 in the United States. (To read a summary of the study for patients, click here.)

“We did this study to formally test whether the trial results reflected differences in screening benefit or whether there was a common screening benefit that has somehow been masked by differences in implementation,” Etzioni told Cancer Health.

As reported in The New England Journal of Medicine in 2009, the ERSPC researchers found that PSA-based screening reduced the rate of death from prostate cancer by 20 percent but was associated with a high risk of overdiagnosis. The PLCO researchers found that after seven to 10 years of follow-up, the rate of death from prostate cancer was very low and similar between men who underwent PSA-based screening and digital rectal exams and those who did not.

In both of these studies, participants were randomly assigned to receive prostate cancer screening or not. In the U.S. study, the screening group underwent PSA testing and digital rectal exams every year. In the European study, screening protocols varied across countries, with PSA testing done every four years on average. However, in both studies, some men who were assigned to the screening group did not get it done regularly, while many men assigned to the non-screening group got it done anyway.
The original studies used traditional statistical methods to calculate the effect of screening on the risk of prostate cancer death. Etzioni’s team conducted an extended analysis to estimate the “intensity” of screening, or how much screening actually occurred in each group, regardless of the men’s randomized assignments.

The new analysis found no evidence that prostate screening had different effects in the two trials, but screening intensity was greater and lead time (how much earlier cancer is detected) was longer in the European study, which led to a greater reduction in mortality. Taking these differences into account, screening was associated with a similar risk reduction in the two studies: 25 to 31 percent lower risk in ERSPC and 27 to 32 percent lower risk in PLCO.

“After differences in implementation and settings are accounted for, the ERSPC and PLCO provide compatible evidence that screening reduces prostate cancer mortality,” the study authors concluded.

So Now What?

While Etzioni’s study provides more evidence for the benefits of prostate cancer screening, it did not address the potential harms of overdiagnosis and overtreatment. Andrew Vickers, PhD, of Memorial Sloan Kettering Cancer Center in New York, addressed these risks in an editorial accompanying the study report.

Vickers recommended that providers should stop screening men older than 70, a group that remains the most frequently screened even though they are unlikely to benefit. Follow-up biopsies should be done only when men test PSA positive and are at high risk for aggressive disease. At least half of men found to have cancer after a moderately elevated PSA test have low-grade disease that is unlikely to lead to morbidity or mortality and can be managed conservatively, according to Vickers.

“In summary, PSA-based screening does reduce prostate cancer mortality, but whether this benefit outweighs the harms of overdiagnosis and overtreatment depends on how screening is implemented,” Vickers wrote. “Unfortunately, the way screening has been implemented in the United States leaves much to be desired. The controversy about PSA-based screening should no longer be whether it can do good but whether we can change our behavior so that it does more good than harm.”

The new research findings and USPSTF recommendations won’t satisfy those looking for easy answers. But they offer an opportunity for men to take charge of their health care by learning about the benefits and harms of screening, discussing the pros and cons with their doctors and thinking about how it fits in with their values and preferences.

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