Prostate-Specific Antigen (PSA) Test

Key Points

- The PSA test measures the blood level of PSA, a protein that is produced by the prostate gland. The higher a man’s PSA level, the more likely it is that he has prostate cancer. However, there are additional reasons for having an elevated PSA level, and some men who have prostate cancer do not have elevated PSA.

- The PSA test has been widely used to screen men for prostate cancer. It is also used to monitor men who have been diagnosed with prostate cancer to see if their cancer has recurred (come back) after initial treatment or is responding to therapy.

- Some advisory groups now recommend against the use of the PSA test to screen for prostate cancer because the benefits, if any, are small and the harms can be substantial. None recommend its use without a detailed discussion of the pros and cons of using the test.

1. What is the PSA test?

Prostate-specific antigen, or PSA, is a protein produced by cells of the prostate gland. The PSA test measures the level of PSA in a man’s blood. For this test, a blood sample is sent to a laboratory for analysis. The results are usually reported as nanograms of PSA per milliliter (ng/mL) of blood.

The blood level of PSA is often elevated in men with prostate cancer, and the PSA test was originally approved by the FDA in 1986 to monitor the progression of prostate cancer in men who had already been diagnosed with the disease. In 1994, the FDA approved the use of the PSA test in conjunction with a digital rectal exam (DRE) to test asymptomatic men for prostate cancer. Men who report prostate symptoms often undergo PSA testing (along with a DRE) to help doctors determine the nature of the problem.

In addition to prostate cancer, a number of benign (not cancerous) conditions can cause a man’s PSA level to rise. The most frequent benign prostate conditions that cause an elevation in PSA level are prostatitis (inflammation of the prostate) and benign prostatic hyperplasia (BPH) (enlargement of the prostate). There is no evidence that prostatitis or BPH leads to prostate cancer, but it is possible for a man to have one or both of these conditions and to develop prostate cancer as well.

2. Is the PSA test recommended for prostate cancer screening?

Until recently, many doctors and professional organizations encouraged yearly PSA screening for
men beginning at age 50. Some organizations recommended that men who are at higher risk of prostate cancer, including African American men and men whose father or brother had prostate cancer, begin screening at age 40 or 45. However, as more has been learned about both the benefits and harms of prostate cancer screening (see Questions 5 and 6), a number of organizations have begun to caution against routine population screening. Although some organizations continue to recommend PSA screening, there is widespread agreement that any man who is considering getting tested should first be informed in detail about the potential harms and benefits.

Currently, Medicare provides coverage for an annual PSA test for all Medicare-eligible men age 50 and older. Many private insurers cover PSA screening as well.

3. **What is a normal PSA test result?**

There is no specific normal or abnormal level of PSA in the blood. In the past, most doctors considered PSA levels of 4.0 ng/mL and lower as normal. Therefore, if a man had a PSA level above 4.0 ng/mL, doctors would often recommend a prostate biopsy to determine whether prostate cancer was present.

However, more recent studies have shown that some men with PSA levels below 4.0 ng/mL have prostate cancer and that many men with higher levels do not have prostate cancer (1). In addition, various factors can cause a man’s PSA level to fluctuate. For example, a man’s PSA level often rises if he has prostatitis or a urinary tract infection. Prostate biopsies and prostate surgery also increase PSA level. Conversely, some drugs—including finasteride and dutasteride, which are used to treat BPH—lower a man’s PSA level. PSA level may also vary somewhat across testing laboratories.

Another complicating factor is that studies to establish the normal range of PSA levels have been conducted primarily in populations of white men. Although expert opinions vary, there is no clear consensus regarding the optimal PSA threshold for recommending a prostate biopsy for men of any racial or ethnic group.

In general, however, the higher a man’s PSA level, the more likely it is that he has prostate cancer. Moreover, continuous rise in a man’s PSA level over time may also be a sign of prostate cancer.

4. **What if a screening test shows an elevated PSA level?**

If a man who has no symptoms of prostate cancer chooses to undergo prostate cancer screening and is found to have an elevated PSA level, the doctor may recommend another PSA test to confirm the original finding. If the PSA level is still high, the doctor may recommend that the man continue with PSA tests and DREs at regular intervals to watch for any changes over time.

If a man’s PSA level continues to rise or if a suspicious lump is detected during a DRE, the doctor may recommend additional tests to determine the nature of the problem. A urine test may be recommended to check for a urinary tract infection. The doctor may also recommend imaging tests, such as a transrectal ultrasound, x-rays, or cystoscopy.

If prostate cancer is suspected, the doctor will recommend a prostate biopsy. During this
procedure, multiple samples of prostate tissue are collected by inserting hollow needles into the prostate and then withdrawing them. Most often, the needles are inserted through the wall of the rectum (transrectal biopsy); however, the needles may also be inserted through the skin between the scrotum and the anus (transperineal biopsy). A pathologist then examines the collected tissue under a microscope. The doctor may use ultrasound to view the prostate during the biopsy, but ultrasound cannot be used alone to diagnose prostate cancer.

5. **What are some of the limitations and potential harms of the PSA test for prostate cancer screening?**

**Detecting prostate cancer early may not reduce the chance of dying from prostate cancer.** When used in screening, the PSA test can help detect small tumors that do not cause symptoms. Finding a small tumor, however, may not necessarily reduce a man’s chance of dying from prostate cancer. Some tumors found through PSA testing grow so slowly that they are unlikely to threaten a man’s life. Detecting tumors that are not life threatening is called “overdiagnosis,” and treating these tumors is called “overtreatment.”

Overtreatment exposes men unnecessarily to the potential complications and harmful side effects of treatments for early prostate cancer, including surgery and radiation therapy. The side effects of these treatments include urinary incontinence (inability to control urine flow), problems with bowel function, erectile dysfunction (loss of erections, or having erections that are inadequate for sexual intercourse), and infection.

In addition, finding cancer early may not help a man who has a fast-growing or aggressive tumor that may have spread to other parts of the body before being detected.

**The PSA test may give false-positive or false-negative results.** A false-positive test result occurs when a man’s PSA level is elevated but no cancer is actually present. A false-positive test result may create anxiety for a man and his family and lead to additional medical procedures, such as a prostate biopsy, that can be harmful. Possible side effects of biopsies include serious infections, pain, and bleeding.

Most men with an elevated PSA level turn out not to have prostate cancer; only about 25 percent of men who have a prostate biopsy due to an elevated PSA level actually have prostate cancer (2).

A false-negative test result occurs when a man’s PSA level is low even though he actually has prostate cancer. False-negative test results may give a man, his family, and his doctor false assurance that he does not have cancer, when he may in fact have a cancer that requires treatment.

6. **What research has been done to study prostate cancer screening?**

Several randomized trials of prostate cancer screening have been carried out. One of the largest is the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, which NCI conducted to determine whether certain screening tests can help reduce the numbers of deaths from several common cancers. In the prostate portion of the trial, the PSA test and DRE were evaluated for their ability to decrease a man’s chances of dying from prostate cancer.

The PLCO investigators found that men who underwent annual prostate cancer screening had a
higher incidence of prostate cancer than men in the control group but the same rate of deaths from the disease (3). Overall, the results suggest that many men were treated for prostate cancers that would not have been detected in their lifetime without screening. Consequently, these men were exposed unnecessarily to the potential harms of treatment.

A second large trial, the European Randomized Study of Screening for Prostate Cancer (ERSPC), compared prostate cancer deaths in men randomly assigned to PSA-based screening or no screening. As in the PLCO, men in ERSPC who were screened for prostate cancer had a higher incidence of the disease than control men. In contrast to the PLCO, however, men who were screened had a lower rate of death from prostate cancer (4).

The United States Preventive Services Task Force has analyzed the data from the PLCO, ERSPC, and other trials and estimated that, for every 1,000 men ages 55 to 69 years who are screened every 1 to 4 years for a decade (5):

- 0 to 1 death from prostate cancer would be avoided.
- 100 to 120 men would have a false-positive test result that leads to a biopsy, and about one-third of the men who get a biopsy would experience at least moderately bothersome symptoms from the biopsy.
- 110 men would be diagnosed with prostate cancer. About 50 of these men would have a complication from treatment, including erectile dysfunction in 29 men, urinary incontinence in 18 men, serious cardiovascular events in 2 men, deep vein thrombosis or pulmonary embolism in 1 man, and death due to the treatment in less than 1 man.

7. **How is the PSA test used in men who have been treated for prostate cancer?**

The PSA test is used to monitor patients who have a history of prostate cancer to see if their cancer has recurred (come back). If a man’s PSA level begins to rise after prostate cancer treatment, it may be the first sign of a recurrence. Such a “biochemical relapse” typically appears months or years before other clinical signs and symptoms of prostate cancer recurrence.

However, a single elevated PSA measurement in a patient who has a history of prostate cancer does not always mean that the cancer has come back. A man who has been treated for prostate cancer should discuss an elevated PSA level with his doctor. The doctor may recommend repeating the PSA test or performing other tests to check for evidence of a recurrence. The doctor may look for a trend of rising PSA level over time rather than a single elevated PSA level.

8. **What does an increase in PSA level mean for a man who has been treated for prostate cancer?**

If a man’s PSA level rises after prostate cancer treatment, his doctor will consider a number of factors before recommending further treatment. Additional treatment based on a single PSA test is not recommended. Instead, a rising trend in PSA level over time in combination with other
findings, such as an abnormal result on imaging tests, may lead a man’s doctor to recommend further treatment.

9. **How are researchers trying to improve the PSA test?**

Scientists are investigating ways to improve the PSA test to give doctors the ability to better distinguish cancerous from benign conditions and slow-growing cancers from fast-growing, potentially lethal cancers. Some of the methods being studied include:

- **Free versus total PSA.** The amount of PSA in the blood that is “free” (not bound to other proteins) divided by the total amount of PSA (free plus bound). Some evidence suggests that a lower proportion of free PSA may be associated with more aggressive cancer.

- **PSA density of the transition zone.** The blood level of PSA divided by the volume of the transition zone of the prostate. The transition zone is the interior part of the prostate that surrounds the urethra. Some evidence suggests that this measure may be more accurate at detecting prostate cancer than the standard PSA test.

- **Age-specific PSA reference ranges.** Because a man’s PSA level tends to increase with age, it has been suggested that the use of age-specific PSA reference ranges may increase the accuracy of PSA tests. However, age-specific reference ranges have not been generally favored because their use may delay the detection of prostate cancer in many men.

- **PSA velocity and PSA doubling time.** PSA velocity is the rate of change in a man’s PSA level over time, expressed as ng/mL per year. PSA doubling time is the period of time over which a man’s PSA level doubles. Some evidence suggests that the rate of increase in a man’s PSA level may be helpful in predicting whether he has prostate cancer.

- **Pro-PSA.** Pro-PSA refers to several different inactive precursors of PSA. There is some evidence that pro-PSA is more strongly associated with prostate cancer than with BPH. One recently approved test combines measurement of a form of pro-PSA called [-2]proPSA with measurements of PSA and free PSA. The resulting “prostate health index” can be used to help a man with a PSA level of between 4 and 10 ng/mL decide whether he should have a biopsy.

**Selected References**


Related Resources

- Understanding Laboratory Tests
- Prostate Cancer
- Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial
- Tumor Markers
- Understanding Prostate Changes: A Health Guide for Men
- What You Need To Know About™ Prostate Cancer
- Prostate Cancer Screening (PDQ®)

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