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# Prostate-Specific Antigen (PSA) Patient Education

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## ABSTRACT

Prostate-specific antigen (PSA) is produced by the prostate gland in men. It plays a crucial role in reproductive health and serves as an invaluable marker for diagnosing various prostate conditions, including enlarged prostate, inflamed prostate, and prostate cancer. The greatest benefit of PSA testing lies not only in the early detection of suspected prostate cancer but also in monitoring the progression of the disease, the response to treatment, and any recurrence. This patient education book provides a comprehensive overview of PSA, incorporating discussions on PSA testing, factors that influence blood PSA levels, and the interpretation of PSA results. It also covers PSA velocity,

PSA doubling time, free and bound PSA, the benefits of PSA testing in prostate cancer management, and the limitations of the PSA test, all explained in simpler terms.

**Keywords:** age and PSA levels; benefits of PSA test in prostate cancer; ethnicity and PSA levels; free and bound PSA; interpretation of PSA results; limitations of PSA test; other factors and blood PSA levels; prostate issues and blood PSA levels; PSA doubling time; PSA testing; PSA velocity

## INTRODUCTION

Prostate-specific antigen, or PSA, is a protein produced by the prostate gland, which is part of the male reproductive system located just below the bladder. PSA serves an essential function: it helps to liquefy semen, facilitating sperm mobility and enhancing reproductive success. While PSA is predominantly found in semen, trace amounts are also present in the blood. Doctors use PSA levels in the blood to assess prostate health. The PSA test is commonly employed to screen for prostate cancer, to monitor the progression of the disease, and to evaluate the effectiveness of its treatment. However, it is important to note that a high PSA level does not necessarily indicate cancer. Other conditions, such as an enlarged prostate or a prostate infection, can also elevate PSA levels. Therefore, PSA serves a dual role in reproductive health and as an indicator of potential prostate issues (1-3). This patient education book provides an overview of PSA functions, the role of PSA testing in detecting prostate problems, and the advantages and disadvantages of PSA testing, all explained in simpler terms.

## THE BIOLOGICAL ROLE OF PSA

On a molecular level, PSA is an enzyme known specifically as a serine protease. Its primary function is to break down proteins, which facilitates the transformation of the seminal coagulum—the thick part of semen—into a more fluid state. This fluidity allows sperm to swim freely toward an egg, enhancing the potential for fertilization. After ejaculation, semen initially forms a gel-like consistency that helps it remain within the female reproductive tract. PSA acts on this gel, breaking down the proteins that give semen its initial coagulated form. This process results in a thinner, more fluid state that is crucial for enabling sperm to navigate toward the egg, thereby increasing the chances of successful fertilization (1-3).

## PSA IN BLOOD

PSA production within the prostate gland is a continuous process, regulated by hormones such as testosterone. This regulation ensures the appropriate amount of PSA is produced to maintain semen liquidity without impacting other bodily functions. Although most PSA is released into semen, a small amount also enters the bloodstream. The primary mechanism by which PSA enters the blood is through natural leakage from the prostate into nearby blood capillaries. This leakage, a normal physiological process, occurs when PSA passes through the tissues that separate the prostate gland from the bloodstream. Consequently, all men have some level of PSA in their blood, a fact that can be assessed through a PSA test.

## PSA TESTING

PSA testing is a medical procedure that measures the level of prostate-specific antigen (PSA) in the blood. The test is straightforward and involves drawing a small blood sample from a vein, typically in the arm. The procedure is quick, usually taking just a few minutes, and can be performed in a doctor's office or a lab. After the blood is collected, it is sent to a laboratory for analysis to determine the amount of PSA present. The results are reported as the concentration of PSA in the blood, measured in nanograms per milliliter (ng/mL). Normal PSA levels generally range from 0 to 4 ng/mL. A PSA level within this range usually indicates a lower likelihood of prostate issues. However, it is important to recognize that 'normal' levels can vary based on a variety of factors, as will be discussed further.

### Age and PSA Levels

PSA levels naturally vary with age. As men grow older, their prostate gland often enlarges—a condition known as benign prostatic hyperplasia (BPH)—which can lead to higher PSA levels. Consequently, older men generally have higher PSA levels compared to younger men. To obtain a clearer picture, age-specific PSA levels are used, providing benchmarks for what is considered a normal range of PSA in the blood at different ages. This is crucial as it recognizes that PSA levels can naturally increase with age, aiding in the differentiation between normal age-related changes and potential health issues. For instance, the recommended PSA levels are typically stratified by age: for men aged 40 to 49 years, a normal PSA level might range from 0 to 2.5 ng/mL; for those 50 to 59 years, the range might extend up to 3.5 ng/mL; for men aged 60 to 69 years, normal levels can go up to 4.5 ng/mL; and for those over 70, up to 6.5 ng/mL might still be considered normal. These thresholds help

doctors better interpret PSA test results, reducing the likelihood of unnecessary investigations for older men while maintaining vigilance for potential prostate issues across all age groups.

## Ethnicity and PSA Levels

Ethnicity can influence PSA levels, with certain racial and ethnic groups typically exhibiting different average PSA levels. For example, African-American men often have higher average PSA levels compared to Caucasian and Hispanic men. This observation is based on studies primarily conducted in the United States, leading to the specific reference to African-American men. It is reasonable to interpret this as suggesting that men of black race generally have higher average PSA levels than men from other ethnic groups. Understanding these variations is crucial for providing accurate diagnoses and ensuring that prostate cancer screening is appropriately tailored to individual risk profiles based on ethnicity.

## Prostate Issues and PSA Blood Levels

Normal levels of PSA in the blood can become elevated for several reasons, many of which are related to changes in the prostate gland. Benign prostatic hyperplasia (BPH), a non-cancerous enlargement of the prostate that tends to occur as men age, is one common cause of increased PSA levels. Prostate infections or inflammation, known as prostatitis, can also cause PSA levels to rise. These conditions cause the prostate to swell and increase the permeability of prostate tissue, allowing more PSA to leak into the bloodstream. Additionally, prostate cancer can elevate PSA levels because cancer cells produce more PSA than normal cells.

## Other Factors Affecting Blood PSA Levels

In addition to medical conditions, certain activities and circumstances can temporarily raise PSA levels. Physical activities that exert pressure on the prostate, such as bike riding, or medical procedures that involve the prostate, can lead to temporarily higher PSA levels. Similarly, ejaculating shortly before a PSA test can result in a slight elevation in PSA levels. Medications also influence PSA levels; for example, some drugs used to treat benign prostatic hyperplasia (BPH) can lower PSA levels, potentially masking signs of prostate cancer. Conversely, some hormone treatments or therapies may elevate PSA levels. The impact of lifestyle factors and diet on PSA levels has also been studied, though the findings are less conclusive.

Given these variables, elevated PSA levels are not specific to cancer alone but suggest that further investigation is necessary to determine the underlying cause.

## INTERPRETATION OF PSA RESULTS

Given the complexities and various factors that influence PSA levels, interpreting results from blood tests is not always straightforward. Generally, a higher PSA level is considered an indicator of potential prostate issues, which could include prostate cancer, an enlarged prostate, or a prostate infection. However, there is no specific PSA level that definitively confirms the presence or absence of prostate cancer. Conversely, a low PSA level does not completely rule out prostate problems. Therefore, to gain a clearer picture, additional measures such as PSA velocity, PSA doubling time, and the ratio of free to bound PSA are often considered.

## PSA Velocity

PSA velocity refers to the rate at which PSA levels change over time. Monitoring PSA velocity can provide crucial insights into prostate health, particularly for detecting prostate cancer. It helps doctors not only diagnose prostate cancer but also assess its potential aggressiveness, aiding in tailoring appropriate treatment strategies. PSA velocity is calculated by measuring the change in PSA levels between two tests and dividing this difference by the time interval between those tests, expressed in ng/mL per month or year.

For example, if a man's PSA level is measured at 4 ng/mL in January and then again at 6 ng/mL in June of the same year, the change in PSA level is 2 ng/mL over 5 months. To calculate the PSA velocity, divide the total change by the number of months, yielding 0.4 ng/mL per month. This calculation provides a clear numerical rate at which PSA levels are increasing, crucial for assessing the progression of prostate-related conditions. A rapid increase, such as a significant rise within just a few months, can indicate a higher risk of aggressive prostate cancer. Generally, a PSA velocity greater than 0.75 ng/mL per year might prompt further diagnostic investigation, especially in the presence of other risk factors for prostate cancer.

## PSA Doubling Time

PSA doubling time measures how quickly the level of PSA in the blood is doubling, serving as an important indicator of the progression and aggressiveness of prostate cancer. A shorter doubling time is generally associated with a higher risk of cancer progression and a worse prognosis. For example, if a man's PSA level increases from 4 ng/mL to 8 ng/mL from January to April, the doubling has occurred over three months. Therefore, the PSA doubling time in this case

would be three months. This relatively short doubling time suggests rapid disease progression, indicating that the prostate cancer may be aggressive and could require more urgent or intensive treatment approaches.

## Free and Bound PSA

In the context of prostate health, PSA is present in the blood in two main forms: free PSA and bound PSA. Free PSA circulates in the blood unattached to other proteins, while bound PSA is attached to blood proteins, aiding its transport through the bloodstream. The balance between these two forms is crucial in prostate cancer screening and diagnosis.

Typically, a total PSA test measures both free and bound PSA without distinguishing between them. However, if the total PSA level is elevated, further testing can differentiate these forms through a free PSA test, which measures the ratio of free PSA to total PSA. A lower ratio often suggests a higher likelihood of prostate cancer, while a higher ratio may indicate benign conditions such as benign prostatic hyperplasia (BPH) or an enlarged prostate.

Consider a scenario where a man's total PSA level is 10 ng/mL. If a test specifically measuring free PSA reports 2 ng/mL, the free PSA ratio is calculated by dividing the free PSA level by the total PSA level. In this example, the free PSA ratio would be 20% ( $2 \text{ ng/mL free PSA} / 10 \text{ ng/mL total PSA}$ ).

A free PSA ratio of 20% is considered low, indicating a higher probability of prostate cancer. Typically, a free PSA ratio below 25% suggests a greater likelihood of cancer, while ratios above 25% are more indicative of benign conditions such as an enlarged prostate. In this case, with a free PSA ratio of 20%, a doctor might recommend further diagnostic



procedures, such as a biopsy, to investigate the possibility of prostate cancer more thoroughly.

## BENEFITS OF PSA TESTING IN PROSTATE CANCER

PSA testing for prostate cancer detection offers significant benefits. Its primary advantage is the ability to detect prostate cancer early. Elevated PSA levels can signal the presence of prostate issues, including cancer, before symptoms appear. *Early detection* is critical because it enables early intervention, which is often less invasive and more effective, potentially saving lives and improving long-term health outcomes.

Another crucial aspect of PSA testing is *monitoring prostate cancer treatment* and detecting any recurrence of the disease. PSA levels are highly sensitive to changes in prostate activity, making them an invaluable tool in managing prostate health after a diagnosis. Following a diagnosis, the primary goal is to eliminate the cancer or control its growth. During treatment, regular PSA tests help doctors assess the effectiveness of the treatment. A decrease in PSA levels typically indicates that the cancer is responding well to treatment, whether through surgery, radiation, hormone therapy, or a combination of these. Conversely, stable or increasing PSA levels may suggest that the treatment is not effective, prompting a reassessment of treatment strategies.

Ongoing monitoring after successful initial treatment is crucial to detect any signs of *recurrence*. Regular PSA testing is part of this surveillance effort. An increase in PSA levels after treatment completion can be an early indicator of prostate cancer recurrence. Early detection of a

recurrence is vital as it allows for timely intervention, which may include additional treatments or changes in therapy to manage the cancer effectively.

This monitoring process is typically lifelong for men who have been treated for prostate cancer. The frequency of PSA tests varies based on factors such as the initial severity of the cancer, the treatments used, and the outcomes of previous tests. The aim is to maintain vigilance for any changes that might suggest the cancer has returned or progressed, while balancing the need to avoid excessive testing or causing undue anxiety.

## LIMITATIONS OF THE PSA TEST

The PSA test is not without its limitations. One major challenge is that elevated PSA levels do not necessarily indicate the presence of prostate cancer. High PSA levels can also be caused by other prostate conditions such as benign prostatic hyperplasia (enlarged prostate) or prostatitis (inflammation of the prostate). This can lead to false-positive results, where the test suggests cancer might be present when it is not, causing unnecessary stress for patients and potentially leading to further invasive tests like biopsies, which carry their own risks.

Another limitation is the potential for false negatives, where PSA levels appear normal despite the presence of cancer. This can falsely reassure patients and potentially delay proper diagnosis and treatment. Moreover, the PSA test struggles to distinguish between aggressive and less aggressive forms of prostate cancer. Detecting slow-growing tumors that may never cause significant harm can result in overdiagnosis and overtreatment, including

surgeries and therapies that might have a more detrimental impact on quality of life than the cancer itself.

Additionally, there is no consensus on the PSA levels that should trigger concern. There is no universally accepted "normal" or "abnormal" PSA value, as levels can vary significantly due to factors such as age, race, and individual medical history. This variability complicates the interpretation of PSA test results and decision-making regarding further testing and treatment.

These controversies have led to varied guidelines on PSA screening. Some health organizations recommend routine screening for certain age groups, while others advise against it, suggesting that the decision to undergo PSA screening should be made on an individual basis after discussing the potential risks and benefits with a healthcare provider. The debate continues, with ongoing research aimed at refining PSA screening practices to maximize the benefits of detecting aggressive cancers early while minimizing unnecessary treatments for less harmful conditions.

## CONCLUSION

PSA testing has become a cornerstone in assessing prostate health and managing conditions related to the prostate gland, particularly prostate cancer. While its primary use is to screen for prostate cancer, the significance of PSA testing extends beyond this singular application. It is a critical tool for early detection, which can lead to timely and potentially life-saving treatments. PSA testing is also essential for monitoring the effectiveness of prostate cancer treatments and detecting any recurrence of the disease.

Despite its widespread use, PSA testing is not without controversies and limitations. The interpretation of PSA levels can be complex; elevated levels can result from a variety of factors other than cancer, such as benign prostatic hyperplasia, prostatitis, and even recent physical activities. This complexity can lead to false positives or negatives, potentially causing unnecessary anxiety or delaying appropriate treatment. Therefore, it is crucial to consider PSA levels alongside other diagnostic tools and personal health factors to provide a more accurate assessment of prostate health.

Despite the controversies, and the pros and cons, PSA testing has been a lifesaver for many men. It has played a pivotal role in identifying issues with the prostate gland, especially prostate cancer, enabling early interventions that lead to beneficial outcomes.

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