

Cancer Association of South Africa (CANSA)



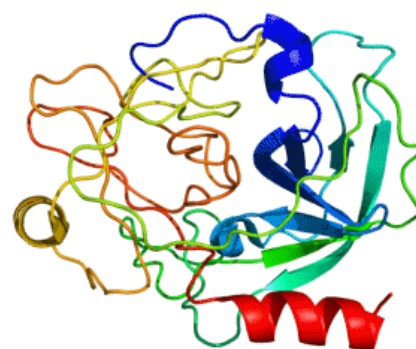
Research • Educate • Support

Fact Sheet on the Role of Prostate Specific Antigen (PSA) Screening on Prostate Cancer Diagnosis and Treatment

Introduction

Prostate Specific Antigen (PSA) is a glycoprotein enzyme exclusively produced by the epithelial cells of the prostate gland. PSA is a member of the kallikrein-related peptidase family.

PSA is produced for the ejaculate, where it liquefies semen to allow sperm to swim freely. It is also believed to create the correct pH balance for sperm to survive and also instrumental in dissolving cervical mucus, allowing easy entry of sperm into the uterus.



[Picture Credit: PSA]

Incidence of Prostate Cancer in South Africa

According to the outdated National Cancer Registry (2014), known for under reporting, the following number of prostate cancer cases was histologically diagnosed in South Africa during 2014:

Group - Males 2014	No of Cases	Lifetime Risk	Percentage of All Cancers
All males	7 057	1:19	19.18%
Asian males	184	1:27	10.79%
Black males	2 833	1:30	25.57%
Coloured males	803	1:14	19.08%
White males	3 238	1:10	15.73%

The frequency of histologically diagnosed cases of prostate cancer in South Africa for 2014 was as follows (National Cancer Registry, 2014):

Group - Males 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	0	1	14	192	1 308	2 717	2 071	593
Asian males	0	0	1	4	25	77	56	12
Black males	0	1	9	90	539	1 065	753	228
Coloured males	0	0	0	22	155	316	232	59
White males	0	0	4	73	572	1 245	992	283

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

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Prostate cancer is caused by changes in the DNA of normal prostate cells. DNA makes up the genes, which control how cells behave. DNA is inherited from one's parents. It is estimated that a small percentage (about 5 to 10%) of prostate cancers are linked to these inherited changes.

Research shows that men with BRCA1/2 mutations are more likely than non-carriers to be diagnosed with advanced-stage prostate cancer or cancer that had already spread.

Prostate Specific Antigen

Prostate Specific Antigen (PSA) is a protein produced by normal prostate cells. This enzyme participates in the dissolution of the seminal fluid coagulum and plays an important role in fertility. The highest amounts of PSA are found in seminal fluid; some PSA escapes the prostate and can be found in the blood serum.

Rising levels of PSA in serum are associated with prostate cancer. The PSA level also tends to rise in men with benign prostatic hyperplasia (enlargement of the prostate) and is a good marker for prostate volume. PSA levels are usually also elevated in men with acute bacterial prostatitis (inflammation of the prostate).

Nordström, T., Akre, P. Aly, M., Grönberg, H. & Eklund, M. 2018.

Background: Screening for prostate cancer using prostate-specific antigen (PSA) alone leads to unnecessary biopsying and overdiagnosis. PSA density is easily accessible, but early evidence on its use for biopsy decisions was conflicting and use of PSA density is not commonly recommended in guidelines.

Methods: We analyzed biopsy outcomes in 5291 men in the population-based STHLM3 study with PSA ≥ 3 ng/ml and ultrasound-guided prostate volume measurements by using percentages and regression models. PSA density was calculated as total PSA (ng/ml) divided by prostate volume (ml). Main endpoint was clinically significant cancer (csPCa) defined as Gleason Score ≥ 7 .

Results: The median PSA-density was 0.10 ng/ml² (IQR 0.075-0.14). PSA-density was associated with the risk of finding csPCa both with and without adjusting for the additional clinical information age, family history, previous biopsies, total PSA and free/total PSA (OR 1.06; 95% CI:1.05-1.07 and OR 1.07, 95% CI 1.06-1.08). Discrimination for csPCa was better when PSA density was added to a model with additional clinical information (AUC 0.75 vs. 0.73, $P < 0.05$). The proportion of men with Gleason Score 6 (ISUP 1) was similar across stratas of PSA-density. Omitting prostate biopsy for men with PSA-density ≤ 0.07 ng/ml² would save 19.7% of biopsy procedures, while missing 6.9% of csPCa. PSA-density cutoffs of 0.10 ng/ml² and 0.15 ng/ml² resulted in detection of 77% (729/947) and 49% (461/947) of Gleason Score ≥ 7 tumors.

Conclusions: PSA-density might inform biopsy decisions, and spare some men from the morbidity associated with a prostate biopsy and diagnosis of low-grade prostate cancer.

What Every Man Should Know About PSA screening

- Screening does not lower one's risk of having prostate cancer; it increases the chance that one will find out that one has it
- PSA testing can detect early-stage cancers that a digital rectal examination (DRE) would miss
- A "normal" PSA level of 4 ng/ml or below does not guarantee that one is cancer-free; in about 15% of men with a PSA below 4 ng/ml, a biopsy will reveal prostate cancer

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- A high PSA level may prompt one to seek treatment, resulting in possible prevention of urinary and sexual side effects
- Conditions other than cancer – non-cancerous enlargement of the prostate (BPH) and prostatitis (inflammation of the prostate), for example, can elevate one’s PSA level

PSA testing guidelines from the American Cancer Society emphasise discussing the pros and cons of prostate cancer screening with one’s doctor, including one’s individual level of prostate cancer risk, before having a PSA blood test.

The Prostate Specific Antigen Screening Debate

The purpose of screening is to detect prostate cancer at its earliest stages, before any symptoms have developed. Some men do experience symptoms that might indicate the presence of prostate cancer. These symptoms can also indicate the presence of other prostate diseases or disorders (such as non-cancerous enlargement of the prostate (BPH) or inflammation of the prostate), so these men will undergo a more thorough work-up.

Typically, prostate cancer that’s detected by screening is in the very early-stages and can be treated most effectively. Physicians can screen for prostate cancer quickly and easily in their office using two tests: the PSA (prostate-specific antigen) blood test and the digital rectal exam (DRE).

The PSA Blood Test - PSA is a protein produced by cells within the prostate and released in very small amounts into the bloodstream. When there is a problem with the prostate—like the development and growth of prostate cancer—more and more PSA is released. It eventually reaches a level where it can be easily detected in the blood.

For a PSA test, a small amount of blood is drawn from the arm, and the level of PSA is measured:

- Levels under 4 ng/mL are usually considered “normal.”
- Levels over 10 ng/mL are usually considered “high”
- Levels between 4 and 10 ng/mL are usually considered “intermediate.”

PSA is not a perfect test. Levels can be elevated if other prostate problems are present, such as BPH or prostatitis (inflammation of the prostate). Some men with prostate cancer may even have low levels of PSA. PSA can also be diluted in men who are overweight or obese, due to a larger blood volume, and a prostate biopsy at a relatively lower number (i.e. 3.5 instead of 4) should be considered.

The Digital Rectal Examination - During a DRE, the physician inserts a gloved, lubricated finger into the rectum and examines the prostate for any irregularities in size, shape, and texture. Often, the DRE can be used by urologists to help distinguish between prostate cancer and non-cancerous conditions such as BPH.



[Picture Credit: Digital Rectal Examination]

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Important to Note - Many men will be found to have cancer even with “normal” results from the PSA test and DRE.

The decision about what to do next in this circumstance is usually based on the patient’s age, other risk factors, and the specifics of the type of cancer (grade, stage, etc).

Scott, E. & Munkley, J. 2019.

Prostate cancer is the most commonly diagnosed malignancy in men, claiming over 350,000 lives worldwide annually. Current diagnosis relies on prostate-specific antigen (PSA) testing, but this misses some aggressive tumours, and leads to the overtreatment of non-harmful disease. Hence, there is an urgent unmet clinical need to identify new diagnostic and prognostic biomarkers. As prostate cancer is a heterogeneous and multifocal disease, it is likely that multiple biomarkers will be needed to guide clinical decisions. Fluid-based biomarkers would be ideal, and attention is now turning to minimally invasive liquid biopsies, which enable the analysis of tumour components in patient blood or urine. Effective diagnostics using liquid biopsies will require a multifaceted approach, and a recent high-profile review discussed combining multiple analytes, including changes to the tumour transcriptome, epigenome, proteome, and metabolome. However, the concentration on genomics-based parameters for analysing liquid biopsies is potentially missing a goldmine. Glycans have shown huge promise as disease biomarkers, and data suggests that integrating biomarkers across multi-omic platforms (including changes to the glycome) can improve the stratification of patients with prostate cancer. A wide range of alterations to glycans have been observed in prostate cancer, including changes to PSA glycosylation, increased sialylation and core fucosylation, increased O-GlcNAcylation, the emergence of cryptic and branched N-glycans, and changes to galectins and proteoglycans. In this review, we discuss the huge potential to exploit glycans as diagnostic and prognostic biomarkers for prostate cancer, and argue that the inclusion of glycans in a multi-analyte liquid biopsy test for prostate cancer will help maximise clinical utility.

Actor Ben Stiller on PSA Testing

Actor Ben Stiller is crediting a prostate cancer screening test for saving his life, revealing today that he was diagnosed and treated for prostate cancer two years ago. But should all men get this screening test?

In an interview on The Howard Stern Show recently, Stiller revealed for the first time that he was diagnosed with prostate cancer at age 48. The actor, who is now 50, said doctors detected the cancer because Stiller had undergone a prostate-specific antigen test, or PSA test, which looks for levels of the protein PSA in the blood. Abnormally high levels of PSA in the blood can mean that a man has prostate cancer, but not always. In Stiller's case, a follow-up MRI and biopsy showed he had prostate cancer.

"This thing saved my life," Stiller said of the PSA test.

The PSA test is the main test used to screen for prostate cancer, but it is controversial. In 2012, the U.S. Preventive Services Task Force, or USPSTF (an expert panel that advises the federal government) recommended that men not undergo routine screening for prostate cancer with the PSA test, no matter their age.

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The American Cancer Society have since changed their stance and now recommends that men have a discussion with their doctor about whether to start PSA screening at age 50 if they are at average risk for prostate cancer, and at age 40 to 45 if they have a family history of prostate cancer.

PSA Testing Saves Lives

An analysis of two influential studies of prostate cancer screening conducted in 2017 concludes that the much-debated PSA test “significantly” reduces deaths from the Prostate Cancer, suggesting that current recommendations against routine PSA screening might be steering men away from a lifesaving procedure (Bornman, 2015; Eetzioni, 2017).

Advantages of Prostate Specific Antigen Screening in South Africa

Studies related to increased prostate cancer incidence and associated mortality, decreased age at diagnosis and aggressive pathological/biochemical presentation has not sufficiently been studied in South Africa. Initiated in 2008, the Southern African Prostate Cancer Study (SAPCS) is a unique ongoing resource to investigate clinical presentation and risk factors within South African black populations. Data from this study suggest that lack of PSA testing, in particular the more rural localities, is contributing to aggressive presentation of prostate cancer at a late stage. The research shows that men in Limpopo Province present almost 3 years later than what is found in other parts of the world.

The lack of PSA screening in remote areas results in lack of options for surgical intervention with less than 2% of the SAPCS being suitable for radical prostatectomy. The study further showed that there is a need for expansion to further elucidate the contributing factors driving aggressive disease. (Bornman, 2015).

The Nigeria experience – in a recent study by Akinremi, *et al.*, (2014) in Nigeria, it was concluded that PSA screening is very important to better define the prostate cancer prevalence and characteristics in the population; otherwise political and economic circumstances will ensure that men still present late with aggressive prostate cancer.

Non-Cancer Causes of a Raised PSA Test

High PSA levels from prostatitis – “The PSA test is a good screening tool for prostate cancer, but it is not very specific,” says Erik P. Castle, MD, FACS, an associate professor of urology at the Mayo Clinic. “Common causes of inflammation in the gland, called prostatitis, can cause high PSA levels.” Prostatitis caused by bacteria can be treated with antibiotics. Another more common type of prostatitis, called nonbacterial prostatitis, can be harder to treat and last a long time. Prostatitis is the most common prostate problem for men younger than 50.

High PSA levels from medical procedures - “Anything that traumatically interferes with the architecture around the prostate gland can make PSA go up,” says John Milner, MD, FRCS, an assistant professor of urology at Loyola University's Stritch School of Medicine in Chicago. “One of the most common causes of significantly high PSA from this type of trauma is the placing of a catheter into the bladder.” Another cause is a prostate or bladder examination that involves passing

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a scope or taking a biopsy. "Since it takes about two to three days for PSA to go down by half, one should wait about two to three weeks after this type of trauma to do a PSA test."

High PSA levels from BPH – Benign prostate hyperplasia (BPH), is an enlargement of the prostate gland, but it is not prostate cancer. "BPH means more cells, so that means more cells making PSA," explains Dr. Castle. BPH may not need to be treated unless it is causing frequent or difficult urination. BPH is the most common prostate problem in men over age 50. One's doctor may be able to tell the difference between BPH and prostate cancer by doing a digital rectal exam. BPH usually causes abnormal PSA tests in the 4 to 10 range.

High PSA levels from a urinary tract infection - "Any infection near the prostate gland, including a urinary tract infection, can irritate and inflame prostate cells and cause PSA to go up," says Dr. Milner. If you've been diagnosed with a urinary tract infection, be sure to wait until after the infection has cleared up before getting a PSA test. In men, most urinary tract infections are caused by bacteria and respond well to antibiotics. Be on the alert: BPH increases your risk for a urinary tract infection.

High PSA levels as one gets older - Even without any prostate problems, your PSA levels can go up gradually as you age. "At age 40, a PSA of 2.5 is the normal limit," says Milner. "By age 60, the limit is up to 4.5; by age 70, a PSA of 6.5 could be considered normal." Even so, a study done in Sweden and reported in the medical journal *BMJ* found that a low PSA at age 60 is especially welcome news. In 1,167 men who were followed from age 60 to age 85, those with a PSA at or below 1 ng/ml at age 60 had only a 0.2 percent chance of dying from prostate cancer.

High PSA levels after ejaculation - "Ejaculation can cause an elevation of one's PSA level, and so can having a digital rectal exam (DRE)," explains Milner. "These types of PSA elevations are usually not enough to make a significant difference unless one's PSA is borderline. PSA should return to normal in two to three days." Doctors will usually draw blood for a PSA level before doing a rectal exam. Ask your doctor if you should avoid ejaculation for a few days before a PSA test.

High PSA levels from riding one's bike - There have been occasional studies that link prolonged bike riding to an increase in PSA levels, but others haven't found such a connection. "You would probably have to be a Lance Armstrong-type bike rider to worry about bike riding and a significant rise in your PSA," says Castle. "The most important thing to know about PSA is that it is still a really important screening test for prostate cancer, and prostate cancer is still the number two cancer killer behind lung cancer for men." (Every Day Health).

To Have a PSA Screening Test or Not

Making the decision to have a PSA test depends on a variety of factors. Here are some tips that can help in making a good decision.

Cancer screening tests - including the prostate-specific antigen (PSA) test to look for signs of prostate cancer - can be a good idea. Prostate cancer screening can help identify cancer early on, when treatment is most effective. And a normal PSA test, combined with a digital rectal exam, can help reassure one that it is unlikely one has prostate cancer. But getting a PSA test for prostate cancer may not be necessary for some men, especially men 75 and older.

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Professional organisations vary in their recommendations about who should - and who should not - get a PSA screening test. While some have definitive guidelines, others leave the decision up to men and their doctors. Organisations that do recommend PSA screening generally encourage the test in men between the ages of 40 and 75, and in men with an increased risk of prostate cancer.

Ultimately, whether one has a PSA test is something one should decide after discussing it with one's doctor, considering one's risk factors and weighing one's personal preferences. A simple test, not-so-simple decision - there are a number of pros and cons to the PSA test.

Pros of PSA Screening	Cons of PSA Screening
PSA screening may help one detect prostate cancer early	Some prostate cancers are slow growing and never spread beyond the prostate gland.
Cancer is easier to treat and is more likely to be cured if it is diagnosed in the early stages of the disease.	Not all prostate cancers need treatment. Treatment for prostate cancer may have risks and side effects, including urinary incontinence, erectile dysfunction and bowel dysfunction.
PSA testing can be done with a simple, widely available blood test.	PSA tests are not fool proof. It is possible for one's PSA levels to be elevated when cancer is not present, and to not be elevated when cancer is present.
For some men, knowing is better than not knowing. Having the test can provide one with a certain amount of reassurance – either that one probably do not have prostate cancer or that one does have it and can now have it treated.	A diagnosis of prostate cancer can provoke anxiety and confusion. Concern that the cancer may not be life-threatening can make decision making complicated.
The number of deaths from prostate cancer has gone down since PSA testing became available.	It is not yet clear whether the decrease in deaths from prostate cancer is due to early detection and treatment based on PSA testing or due to other factors.

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