Cancer Association of South Africa (CANSA)

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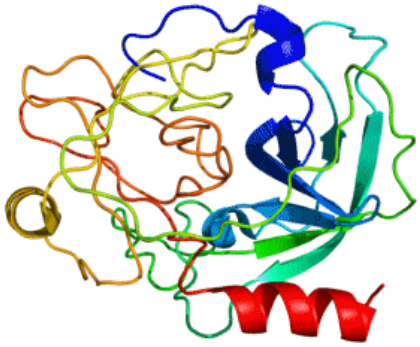
Fact Sheet on the Role of Prostate Specific Antigen (PSA) Screening on Prostate Cancer Diagnosis and Treatment

Introduction

Prostate Specific Antigen (PSA), also known as gamma-seminoprotein or kallikrein-3 (KLK3), is a glycoprotein enzyme encoded in humans by the *KLK3* gene. PSA is a member of the kalllikrein-related peptidase family and is secreted by the epithelial cells of the prostate gland.

PSA is produced for the ejaculate, where it liquefies semen in the seminal coagulum and allows sperm to swim freely. It is also believed to be instrumental in dissolving cervical mucus, allowing the entry of sperm into the uterus.
(Wikipedia).



[Picture Credit: PSA]

Incidence of Prostate Cancer in South Africa

According to the National Cancer Registry (2011) the following number of prostate cancer cases was histologically diagnosed in South Africa during 2011:

Group - Males 2011	No of Cases	Lifetime Risk	Percentage of All Cancers
All males	6 143	1:19	19.07%
Asian males	125	1:38	19.64%
Black males	2 448	1:30	19.34%
Coloured males	702	1:15	18.22%
White males	2 868	1:10	16.17%

The frequency of histologically diagnosed cases of prostate cancer in South Africa for 2011 was as follows (National Cancer Registry, 2011):

Group - Males 2011	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	3	2	7	173	1 187	2 328	1 837	555
Asian males	0	0	0	3	25	51	36	9
Black males	1	2	6	71	494	850	743	239
Coloured males	1	0	0	18	144	293	187	56
White males	1	0	1	81	524	1 134	871	251

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.

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

Research shows that men with BRCA1/2 mutations were 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).

Since 1986, when tests for measuring PSA levels in serum were introduced into clinical practice, early diagnosis and management of prostate cancer has been revolutionised, and much has been learned about the strengths and weaknesses of these assays. PSA testing not only helps identify men in whom a prostate biopsy would be appropriate but also assists in assessing the response to therapy, determining tumour progression, and, in its most controversial role, screening for prostate cancer.

Around three quarters of men (76%) with a raised PSA level do not have prostate cancer and some men with a normal PSA level do have prostate cancer. 1 in 50 men (2%) with fast-growing prostate cancer have a normal PSA level.
(Medscape; WebMD; Prostate Cancer UK).

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

- A high PSA level may prompt one to seek treatment, resulting in possible 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

In the past few years, more and more men who undergo PSA screening and later learn that they have cancer have opted to pursue active surveillance. This strategy involves frequent monitoring of the disease through PSA tests and biopsies - and postponing treatment until the cancer shows signs of increasing its activity. In short, these men choose to live with prostate cancer until it advances, sometimes avoiding potentially life-altering side effects for several years.

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.
(Harvard Medical School).

Differences in Access to Health Care
People in poor countries tend to have less access to health services than those in better-off countries, and within countries, the poor have less access to health services. Although a lack of financial resources or information can create barriers to accessing services, the causal relationship between access to health services and poverty also runs in the other direction. When health care is needed but is delayed or not obtained, people's health worsens, which in turn leads to lost income and higher health care costs, both of which contribute to poverty. Deprivations that lead to ill health are common in developing countries, and the poor in developing countries are particularly at risk. The relationship between poverty and access to health care can be seen as part of a larger cycle, where poverty leads to ill health and ill health maintains poverty.
(Peters, *et al.,* 2008).

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 the prostate and released in very small amounts into the bloodstream. When there's 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.

During 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 biopsy at a relatively lower number (i.e. 3.5 instead of 4) should be considered.

<u>The Digital Rectal Examination</u> - 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]

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 should be based on the patient’s age, other risk factors, and the specifics of the type of cancer (grade, stage, etc).
(Prostate Cancer Foundation).

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.

The American Cancer Society 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.

The main issue with prostate cancer screening is that, although the PSA test can help detect prostate cancer early, it's not clear if the test's benefits outweigh its risks in the long run for most men.
(LiveScience).

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).

Screening for prostate cancer in Europe, using prostate-specific antigen (PSA) levels, has shown that the risk of developing metastatic prostate cancer is reduced by 31% compared with not screening at an average follow-up of 12 years, according to the most recent data to emerge from 4 of the European Randomized Study of Screening for Prostate Cancer (ERSPC) centres.
(Medscape Medical News).

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.

Possible Disadvantages of Prostate Specific Antigen Screening Seen from a First World Perspective
Two long-awaited studies - one conducted in the United States and the other in Europe - were supposed to help settle the debate over the value of PSA testing. Instead, the trials, published in the *New England Journal of Medicine* in March 2009, seemed to come to opposite conclusions. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial reported no survival benefit with PSA screening and digital rectal examination, but the European Randomized Study of Screening for Prostate Cancer (ERSPC) found a 20% reduction in prostate cancer deaths. The ERSPC study estimated that for every life saved, 48 men are treated and 1,068 men are screened.

Although experts are somewhat split on the value of PSA tests as a screening tool, there is widespread agreement on two major points: overdiagnosis and overtreatment rates are far too high, and there is an urgent need to refine PSA testing to be a more effective screening tool. The principal investigator of the Prostate Cancer Prevention Trial and his colleagues wrote an editorial in *The Journal of the American Medical Association* in October 2009 that took a closer look at the issues. They pointed out that while the amount of prostate cancer diagnosed has risen dramatically since PSA testing began, there has not been a proportional decrease in the number of men with metastatic tumours. It appears screening may be detecting a disproportionate number of lower-risk cancers, while missing many of the most aggressive tumors, which may advance too rapidly to be found with periodic testing.

The debate over the effectiveness of PSA screening has quickly filtered into the offices of general practitioners and urologists. On a daily basis, confused men are asking their doctors: "Should I have a PSA test or not?"
(Harvard Medical School).

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 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 you make 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.

Professional organisations vary in their recommendations about who should - and who shouldn't - 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 **- t**here 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 cancde3r 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.

(Mayo Clinic).

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