

Protocol for Conducting a ‘finger-prick’ Prostate Specific Antigen Test

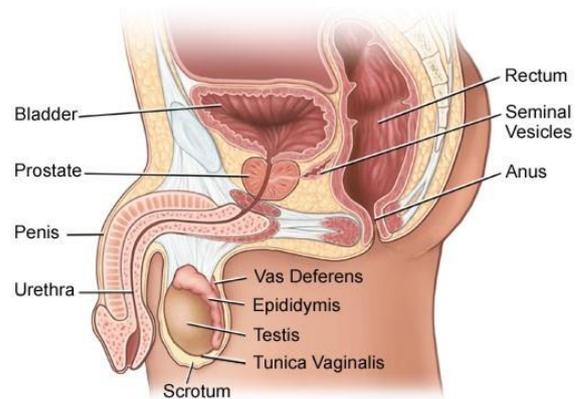
It has been approved that staff in the various CANSA Business Units may conduct the following finger-prick PSA test as part of CANSA’s Men’s Health Programme:

PSA Ultra Prostate Specific Antigen
Semi-Quantitative Rapid Test Single Use Kit
(Whole Blood/Serum/Plasma)

Introduction

The prostate gland is part of the male reproductive system. It is a round gland, about the size of a pea shaped at birth and has the size and shape of walnut in an adult. It lies in the pelvic cavity immediately in front of the rectum. It surrounds the commencement of the urethra (urinary tube) at the base of the urinary bladder. It produces seminal fluid that assists in transporting the sperm during ejaculation.

Prostate cancer is one of the leading cancers in males worldwide. Prostate cancer is currently the second most common malignancy in Black men in South Africa and the most common malignancy in White men in South Africa (excluding skin cancer).



Incidence of Prostate Cancer in South Africa

The following South African statistics regarding histologically diagnosed cases of prostate cancer during 2010 are available from the National Cancer Register (2012):

The following South African statistics regarding prostate cancer are available from the National Cancer Register (2012):

Group 2010	No of Cases	Lifetime Risk	Percentage of All Cancers
All males	6 807	1:19	18,45%
Asian males	155	1:32	18,45%
Black males	2 763	1:30	23,68%
Coloured males	875	1:12	20,17%
White males	3 014	1:11	15,03%

The frequency of histologically diagnosed cases of prostate cancer in South Africa for 2012 was as follows (National Cancer Register, 2012):

Group	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	3	6	103	1 023	2 454	2337	878
Asian males	0	0	0	2	13	56	50	24
Black males	1	2	3	50	422	959	796	328
Coloured males	1	1	0	15	152	296	277	88
White males	1	0	1	31	390	1 042	1 002	389

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.

Like with most cancers, the cause of prostate cancer is not known. However, there are known factors which have been determined through research that increases the risk of men developing prostate cancer.

Guidelines for Having a PSA Test

Routine Prostate Specific Antigen (PSA) testing, at least once every two (2) years, for all males from age 50 is recommended. Men between the ages of 40 and 50 should consider having a PSA test done:

- If they have a family history of prostate cancer
- If they have any of the early or late warning signs of prostate cancer

It is not recommended to conduct routine PSA testing of males over the age of 70 or any man with less than a 10 to 15-year life expectancy unless there are specific indications to do so (WebMD).

Risk Factors for Prostate Cancer

Risk factors for prostate cancer include:

- Age: it occurs more frequently in older men
- Family history: there is often a history of a brother or father who had prostate cancer

- Lifestyle: high fat intake, low consumption of vegetables, obesity, lack of physical activity, and smoking
- Prostate cancer develops in the tissues of the prostate gland and usually grows slowly in comparison with other types of cancer

Early Warning Signs of Prostate Cancer

Early warning signs of prostate cancer include:

- Difficulty in passing urine
- A slow stream, often with dribbling at the end
- Inability to start or stop the flow of urine
- Frequent need to pass urine, especially at night

The symptoms may be related to other factors such as inflammation of the prostate gland called prostatitis or enlargement of the prostate gland (benign prostate hyperplasia) or benign prostatic hypertrophy which are non-cancerous.

Late Warning Signs of Prostate Cancer

Late warning signs of prostate cancer include:

- Inability to pass urine
- Lower back pain
- Blood in the urine or semen
- Painful ejaculation
- Erectile dysfunction
- Weight loss

Prostate Specific Antigen (PSA)

Prostate Specific Antigen (PSA) is made by the prostate gland. Some of it will leak into your blood, and the amount depends on your age and the health of your prostate. Just as important as the PSA number is the trend of that number (whether it is going up, how quickly, and over what period of time). It is important to understand that the PSA test is not perfect.

[Picture Credit: PSA Test]



Raised PSA levels

The amount of PSA in your blood is measured in nanograms of PSA per millilitre of blood (ng/ml). PSA levels can range from 1ng/ml to hundreds of ng/ml.

- A patient aged 50–59, the PSA level is considered raised if it is 3ng/ml or higher
- A patient aged 60–69, the PSA level is considered raised if it is 4ng/ml or higher
- A patient aged 70 or over, the PSA level is considered raised if it is 5ng/ml or higher

A raised PSA level in the blood may show that the individual has a problem with his prostate. However, this may not be prostate cancer. An urinary tract infection may also cause a raised PSA.

Key statistics

About 15% of all men with a 'normal' PSA level (under 4ng/ml) may have prostate cancer.

Two out of three men with a raised PSA level do not have prostate cancer.

One out of three men with a raised PSA level will have cancer.

Two out of three men who have a biopsy do not have cancer.

Biopsies in one in five men fail to spot prostate cancer.

Other conditions, such as an enlarged prostate, prostatitis (inflammation of the prostate), or a urinary infection, can also cause a raised PSA level.

(NHS Choices; eHow; WebMD; Prostate Cancer UK).

Things that Could Raise the PSA Result

PSA is produced by healthy cells in the prostate - it is, therefore, normal for all men to have a small amount of PSA in their blood. There are other things that can raise your PSA level.

- A urinary tract infection – the patient must receive treatment for any infection, and will need to wait around four to six weeks until the infection has cleared up before he has a repeat PSA test
- Vigorous exercise – especially cycling – in the 48 hours before a PSA test
- Ejaculation in the 48 hours before a PSA test
- Anal sex and prostate stimulation – if the person is gay, bisexual or a man who has sex with men, being the receptive partner during anal sex might raise the PSA level. Having the prostate stimulated during sex might also raise the PSA level. It might be worth avoiding this for a week before a PSA test
- A digital rectal examination (DRE) before a PSA test might raise the PSA level
- A prostate biopsy in the six weeks before a PSA test
- Other investigations or operations on the bladder or prostate, or having had a urinary catheter passed. The patient may need to wait up to six weeks after these procedures before having a repeat PSA test

Medications that Could Lower the PSA Reading and Cause a False Negative Result

Finasteride (MK-906, Proscar and Propecia) is a 5 alpha-reductase inhibitor. It works in the prostate by blocking the conversion of testosterone to dihydrotestosterone. This blocking of dihydrotestosterone formation leads to decreases in prostate volume, which in turn leads to a lower level of PSA in the serum. In the prostate cancer patient, men who took finasteride had a 50% decrease in serum PSA level after 1 year of treatment. Therefore, if a patient was taking a 5 alpha-reductase inhibitor such as finasteride (Proscar) or dutasteride (Avodart) for even 1 year, his PSA level would need to be adjusted by multiplying the current value by 2. A man taking finasteride for a full 4 years should have his PSA level multiplied by 2.3 before comparing it with standard reference ranges.

(MedScape).

Different Ways of Looking at Prostate Specific Antigen (PSA)

Prostate Specific Antigen, or PSA for short, is a protein that is produced by prostate cells. The PSA increases as men age, when the prostate enlarges or becomes inflamed and when prostate cancer is present. There are also transient bumps in PSA after, for example, digital rectal examination (DRE), ejaculation, and bike riding. PSA is prostate specific but not cancer specific. There are different ways in which to look at a PSA result.

Absolute Value - when PSA was introduced a cut off of 4.0 was used to achieve what scientists and doctors felt to be an acceptable level of sensitivity (how many it catches) and specificity (how accurate it is if positive). It was soon realised that although this was helpful it missed too many cancers in young men and resulted in too many biopsies and over diagnosis in older men.

Age Based PSA – it is known that PSA rises as one ages. By having a lower cut off in younger men and a higher cut off in older men one is able to catch cancers sooner in the younger population while eliminating a lot of unnecessary biopsies in the older population. There are several accepted reference ranges; one of the most common is this:

Age in Years	Abnormal Value
46 - 55	< 2.5
56 - 65	< 3.5
66 - 75	< 4.5
>75	<6.5

Free and Total PSA - while PSA is a protein that is in the blood stream it is not all existing in the same form. Some is free floating and some is bound to other proteins. It was found that benign disease (not cancerous) tends to have higher levels of free PSA (>25%) and patients with prostate cancer tend to have lower free PSA (<15%). These numbers can help stratify the risk in some men. For example if a patient has a PSA of 8.0 and had a negative biopsy, knowing that he has a PSA free >25% gives one more assurance that he does not have prostate cancer.

PSA Density – it is also known that PSA rises as the prostate gets larger. Men with large prostate glands tend to have higher PSA's. A normal size prostate is about 25 grams. One would consider anything larger than 40 grams an enlarged prostate. A normal PSA density is 0.1 PSA for every gram. This makes sense as a large, 40 gram prostate would have a corresponding upper limit PSA of 4.0. This helps one in men who have had a negative biopsy and have enlarged prostate glands. One is then less likely to worry about someone with a PSA of 6.0 if their prostate is > 60 grams. Conversely, one would be more worried if the PSA is elevated in a smaller prostate (PSA of 4.2 in a 17 gram prostate).

PSA Velocity - one of the most accurate ways of diagnosing prostate cancer is looking at the rate of rise of PSA. A PSA should never go up more than 0.7 points per year. For example, it would probably be better to have a PSA count over 3 checks go from 5.0 to 5.1 to 5.2 than it would be to have the PSA count go from 1.0 to 2.0 to 4.0.

In summary - Prostate Specific Antigen is only a tool. It is far from perfect but it is useful when the patient and his physician work together to make shared decisions. Since the onset of PSA screening the death rate from prostate cancer has almost been cut in half.

Prostate Cancer is still a high cancer killer of men. There is still much to be learned. Getting as much information as possible and making shared decisions with one's doctor will help to understand the risks and benefits of checking one's PSA and what to do with the information.

(Roscoe Nelson, 2014).

Advantages and Disadvantages of Having a PSA Test

There are both advantages and disadvantages that should be considered before a patient agrees to having a PSA test done. It's important you think through the advantages and disadvantages of the PSA test. Having a PSA test is a personal decision – what might be an advantage for one man may not be for another.

Advantages of a PSA Test

- A PSA test can help pick up prostate cancer before any symptoms appear
- A PSA test may help to pick up a fast-growing cancer at an early stage when treatment may stop the cancer spreading and causing problems
- Slow-growing prostate cancer might not need treatment. The patient might be able to have regular check-ups, including PSA tests, to keep an eye on the cancer. This can avoid or delay the side effects of treatment
- Having regular PSA tests could be helpful for men who are more at risk of prostate cancer. This can help spot any changes in the PSA level, which might be a sign of prostate cancer. More research is needed to show how often one might need a test.

Disadvantages of a PSA Test

- The patient might have a raised PSA level, even if he does not have prostate cancer. Around three quarters of men (76 per cent) with a raised PSA level do not have prostate cancer
- If the PSA level is raised the person may need more tests, including a biopsy. The biopsy has some risks, such as pain, infection and blood in the urine and semen. Up to 3 in 50 men (six per cent) may get a serious infection after a biopsy
- The PSA test can miss prostate cancer. 1 in 50 men (two per cent) with fast-growing prostate cancer have a normal PSA level
- The patient might be diagnosed with a slow-growing prostate cancer which would never have caused him any problems or shortened his life. But being diagnosed with cancer could make him worry, and he might decide to have treatment that he did not need
- Treatments for prostate cancer have side effects which can affect one's daily life. These include urinary and bowel problems, and problems getting and keeping an erection

(Prostate Cancer UK).

**PSA Ultra Prostate Specific Antigen
Semi-Quantitative Rapid Test Single Use Kit
(Whole Blood/Serum/Plasma)**

A rapid test for the semi-quantitative detection of prostate specific antigen (PSA) in whole blood.
It is for professional *in vitro* diagnostic use only

This is an extremely sensitive test
The test is not concerned with volume
The test is all about an ACCURATE RATIO between 'blood' and 'buffer'
The test can only be accurate if the ratio between 'blood' and 'buffer' is EXACTLY 2:1
The test, therefore, demands an exact dilution of $\frac{2}{3}$ blood and $\frac{1}{3}$ buffer

There are three (3) lines of the test device:

Line C  Line R  Line T 

Lines C & R must ALWAYS be present
Lines C & R are 'control' lines
Line T is the 'test line'
Line T usually only appears after 5 minutes – NO reading should be taken after expiry of 10 minutes

PROCEDURE FOR PSA TEST

- Provide pre-counselling in line with the CANSA Protocol
- Ask the candidate if he has ever had any treatment for prostate cancer
- **If 'yes', the person does NOT qualify for a finger-prick PSA test**
- Check the expiry date of the test kit – do not use if expired
- The test must remain in the sealed pouch until use
- Do not use the sterile lancet if its protective cap has been removed previously
- No eating, drinking or smoking in the area where the specimens or kits are handled
- Do not use the test if the pouch is damaged in any way
- Don a pair of disposable gloves
- Open the pouch
- Place the test device on a flat and level surface
- Clean the candidate's finger using the alcohol swab
- **Allow the alcohol to dry – do not blow on the finger**
- Remove the protective cap of the lancet
- Push the lancet firmly into the chosen site
- Allow a large drop of free-flowing blood to collect at the puncture site
- **Use the disposable dropper to collect blood**
- There must be no air in the disposable dropper
- Hold the disposable dropper vertical
- Let **two (2) hanging drops of blood** drop into the specimen well (**S**)
- Hold the buffer container vertical and **drop one (1) hanging drop of buffer** into the specimen well (**S**)
- **The drops of blood and buffer must be exactly the same size**
- **The test device MUST NOT be handled or moved at all**
- Wait five (5) minutes and take the reading – timing is VERY important
- No reading should be taken after ten (10) minutes

Result:

Negative

0 – 3 nanogram/mL

3 – 10 nanogram/mL

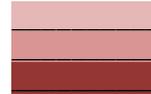
10+ nanogram/mL

No **T** line – both **R** & **C** lines are present

colour of line **T** is lighter than line **R**

colour of line **T** is the same as line **R**

colour of line **T** is darker than line **R**



The test is **invalid** if Control line **C** and Reference Line **R** are not both visible

Protocol for Conducting a PSA Rapid Screening Test

The following protocol should be followed:

Participants:

- must sign an indemnity declaration that provides protection for CANSA and its staff
- are to be informed that the test is a screening test only and that the manufacturers claim a 98% accuracy of test results
- must be counselled on what a positive test result entails
- must also be counselled on what a negative test result entails
- must be counselled both on a pre- and post-test basis
- must be specifically counselled if they have a PSA test result of 4 or higher, making it clear that this does not mean that they necessarily have been tested positive for prostate cancer but that it could merely be an indication of some other form of prostate inflammatory condition (prostatitis), benign prostatic hyperplasia (enlarged prostate), an urinary tract infection, or merely because they are more mature (45 years old or older)

- must be specifically counselled that, even if they have a low PSA test result (a reading of 3 or lower) but have any of the abovementioned warning signs, the possibility of prostate cancer cannot be ruled out completely and that they should visit a medical practitioner to have a serum PSA test as well as a digital rectal examination (DRE)



[Picture Credit: Serum PSA Test]

- must be referred to their regular medical practitioner for follow-up in the event of a PSA result of 4 or higher
- must be referred to their regular medical practitioners for follow-up if they have a PSA result of 3 or lower together with any of the abovementioned warning signs
- residing in remote or rural areas who have a PSA test result of 4 or higher, should have a serum PSA test conducted and be referred to their nearest health care facility with a referral letter together with the PSA test result

Medical Disclaimer

This Protocol is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Protocol. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Protocol.

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Sources and References

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<http://www.nhs.uk/Livewell/Prostatehealth/Pages/psa-test.aspx>

Prostate Cancer UK

<http://prostatecanceruk.org/information/prostate-problems/psa-test>

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<http://www.prostatespecificantigen.net/products.htm>

Serum PSA Test

<http://www.medindia.net/healthnews/prostate-specific-antigen-news.asp>

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<http://www.webmd.com/prostate-cancer/guide/psa>

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