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# Prostate Specific Antigen

## PSA

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This article is for **Medical Professionals**

Professional Reference articles are designed for health professionals to use. They are written by UK doctors and based on research evidence, UK and European Guidelines. You may find the **Prostate Specific Antigen Test (PSA)** article more useful, or one of our other **health articles**.

Treatment of almost all medical conditions has been affected by the COVID-19 pandemic. NICE has issued rapid update guidelines in relation to many of these. This guidance is changing frequently. Please visit

**<https://www.nice.org.uk/covid-19>** to see if there is temporary guidance issued by NICE in relation to the management of this condition, which may vary from the information given below.

Prostate specific antigen (PSA) is a protease whose function is to break down the high molecular weight protein of the seminal coagulum into smaller polypeptides. This action results in the semen becoming more liquid. PSA is produced by epithelial prostatic cells, both benign and malignant. It is also found in the serum. Serum PSA is currently the best method of detecting localised prostatic cancer and monitoring response to treatment but it lacks specificity, as it is also increased in most patients with benign prostatic hyperplasia<sup>[1]</sup>.

# Conditions which may have elevated prostate specific antigen<sup>[2]</sup>

Causes include:

- [Acute urinary retention.](#)
- [Benign prostatic hyperplasia.](#)
- Old age.
- [Prostatitis.](#)
- [Prostate cancer.](#)
- Transurethral resection of the prostate.
- [Urinary catheterisation.](#)

## Normal range

Age-related cut-offs used to be recommended. However, it has since been discovered that age-specific PSA cut-offs are highly variable and may reflect differences in clinical characteristics and demographics of the population<sup>[3]</sup>. As a rule of thumb the normal range is considered to be between 0-4 ng/ml. However, in men aged between 50-69, a PSA of 3.0 ng/ml or higher warrants an urgent referral via the suspected cancer pathway.

## Uses of the prostate specific antigen test in prostate cancer diagnosis



## The national screening debate

A 2015 review by the UK Screening Committee concluded that despite the likelihood that a national screening programme would reduce mortality by at least 21%, the widespread use of PSA in asymptomatic men who had not had a digital rectal examination would increase the risks of over-diagnosing and overtreating clinically insignificant prostate cancers. Men with indolent disease would unnecessarily be exposed to the side-effects of radical treatment, including sexual dysfunction and urinary problems. There is also, in extreme cases, the risk of death.

This position has been confirmed by the ProtecT trial, which demonstrated that there was no difference in 10-year survival rates between men with low-risk localised prostate cancer who were allocated to active surveillance and those who chose radical treatment<sup>[4]</sup>. This was supported by the CAP trial of UK general practices, the findings of which did not support single PSA testing for population-based screening<sup>[5]</sup>.

To complicate matters further, genetic factors (abnormalities of the KLK3 gene) can cause abnormally low PSA readings, resulting in false negatives in some patients<sup>[6]</sup>.

Rather than a national screening programme therefore, a Prostate Cancer Risk Management Programme (PCRMP) has been introduced in the UK. The aim is to provide enough information to primary healthcare professionals to assist asymptomatic men aged 50 and over to make an informed choice about whether or not to have a PSA test<sup>[7]</sup>.

It is hoped that research into emerging biomarkers will eventually result in the PSA test being replaced by more accurate investigations<sup>[8]</sup>.

## Diagnosing individual patients

Public Health England (PHE) realises that there are more than economic and clinical issues to take into account when applying the national policy to individual patients. They have therefore very wisely left it to individual patients to decide, after discussion with their doctor, whether to have a PSA test. PHE have produced summary

information sheets for GPs and asymptomatic men aged 50 and over in order to assist in this process<sup>[9, 10]</sup>.

The patient needs to be apprised of the following points:

- Prostate cancer is only one of several causes of a raised PSA test.
- Three out of four men with a raised PSA will not have cancer cells in their biopsy. Therefore, having the test may lead to unnecessary worry and exposure to the risks of further investigations. The most common problems after biopsy are infection and bleeding. However, if they do not have the test they will have an increased risk of presenting only when they have symptoms, which can increase the chance of prostate cancer remaining undiagnosed until it is advanced and incurable.
- 15% of men with prostate cancer have a normal PSA. Normal results can be falsely reassuring. However, men who do not have the test will miss the chance of early diagnosis and treatment.
- The test cannot distinguish between aggressive and slow-growing cancers and may detect tumours that would not otherwise become evident in the patient's lifetime.
- Potential treatments can include surgery, radiotherapy and hormone therapy. Side-effects can include problems with erections, loss of fertility, and incontinence. Not having the PSA test will mean that treatment will not be required unless symptoms develop, so these risks will be avoided. However, the patient will miss the chance of early detection, as outlined above.

## Monitoring the effects of treatment

There is no conclusive evidence to determine the optimal treatment of localised prostate cancer and many urologists rely on rising PSA results to signal that a radical intervention (usually either chemotherapy or radiotherapy) is necessary. Questions have been raised about the usefulness of PSA levels in making therapeutic decisions.

Studies indicate that the effectiveness of PSA in monitoring treatment varies, and the following should be taken into account<sup>[11]</sup>:

- Short post-treatment PSA doubling time (<3 months in this study) may be useful as a surrogate endpoint for all-cause mortality and prostate cancer-specific mortality after surgery or radiation therapy.
- A PSA reduction of 20% to 40% at three months and 30% or more at two months after initiation of chemotherapy for hormone-independent prostate cancer may be a predictive indicator for overall survival .
- A detectable PSA after radical prostatectomy has been used as an indicator of local treatment failure or metastatic disease. However, trials suggest it should not be the sole criterion on which to decide whether further treatment is indicated.
- PSA alone is less useful in monitoring the effects of radiation therapy and hormonal therapy.

## Practicalities of the prostate specific antigen test

At the time of the test, the patient should not have<sup>[3]</sup>:

- An active urinary tract infection.
- Ejaculated in the previous 48 hours.
- Had a prostate biopsy in the previous six weeks.
- Exercised vigorously in the previous 48 hours.
- Had a recent digital rectal examination (if possible, do the blood test before the examination; otherwise, wait for one week afterwards).
- Gay, bisexual, and other men who have sex with men should avoid receptive anal intercourse for 48 hours before a PSA test.

The specimen should reach the laboratory within 16 hours.

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