Consensus Statement on PSA Testing for Prostate Cancer

This statement was developed for primary care in consultation with Wessex Cancer Alliance (WCA) Primary care group, Wessex Urology Clinical Advisory Group, Dorset Urology Site Specific Group, Wessex Urology GIRFT group and WCA Clinical Reference Group. Guidance is based on currently accepted and peer reviewed research.

Background

Prostate cancer is the most common cancer in males in the UK, accounting for 28% of all new cancers, with 55,100 new cases annually. It is also the second most common cause of cancer death in UK men with around 12,000 deaths per year[1].

Almost 8 in 10 men diagnosed with prostate cancer survive 10 years or more. Survival has tripled in the past 50 years, partly due to PSA testing enabling early diagnosis. However, this can also lead to overdiagnosis which may artificially inflate survival by diagnosing cases which would not have gone on to cause harm in a patient's lifetime.

The challenge is to try to diagnose clinically relevant prostate cancers earlier without over diagnosing cancers which would never have caused clinical problems and to avoid unnecessary over treatment and resulting comorbidity.

What do we know about the risk of developing prostate cancer?

The average lifetime risk for men is 1 in 6. Prostate cancer is much more common in men over the age of 50 years. There are no obvious links to modifiable risk factors, but we know that certain groups have an increased risk of developing prostate cancer and at an earlier age:

- Black men - The risk of developing prostate cancer is increased in black British, African and Caribbean men to 1 in 4 and becomes more common from age 45 years.

- Family history - men who have a first degree relative (father, brother or son) with prostate cancer are 2.5 times more likely to develop prostate cancer. This risk rises to 4 times more likely if two first-degree relatives have prostate cancer. Certain genetic syndromes also increase prostate cancer risk and at a younger age e.g. BRCA and Lynch syndrome. There is also some evidence to suggest that the risk of prostate cancer may be increased in patients with malignant melanoma.

<u>Men without symptoms</u>

PSA testing in men without symptoms has historically been a controversial subject and advice for primary care may change as new research becomes available.

It is important to counsel men who request a PSA test on the pros and cons. NICE guidance suggests PSA testing is associated with 15% false negative results (where a patient has a normal PSA but goes on to be diagnosed with prostate cancer) and up to 75% false positive

results[2]. It may be helpful to use patient resources such as Prostate cancer UK risk checker to inform patients before undergoing testing.

Screening trials have been undertaken using PSA testing as a triage for transrectal prostate biopsy. The European Randomised Study for Screening of Prostate Cancer (ERSPC) monitored 162,000 men aged 55 to 69 over a period of sixteen years with repeated PSA tests and found a 20% relative risk reduction in prostate cancer specific mortality compared with no testing[3]. The UK based Cluster Randomised Trial of a single PSA test for Prostate cancer (CAP)[4] showed 0.09% reduction in prostate cancer deaths after median 15-year follow-up. Both trials were however associated with overdiagnosis of low-risk disease and subsequent overtreatment. They also over-represented white men therefore making it difficult to draw conclusions about black men for whom screening may be more favourable given their increased risk of prostate cancer.

Since these trials the diagnostic pathway has evolved. The introduction of multiparametric MRI (mpMRI) prior to prostate biopsy has allowed much more accurate diagnosis and avoidance of biopsy for many men with elevated PSA associated with benign prostate enlargement. It enables more accurate targeted biopsy and a reduction in associated harm. Active surveillance is now used for low-risk and some favourable intermediate risk cancers and other advancements like focal therapy, robotic surgery and image guided radiotherapy have all lead to reductions in treatment related harms.

The Transform trial[5] is now funded and being set up to compare screening tests including mpMRI and biomarkers in the hope evidence will be established to support a UK national screening programme. However, results will take time and in the meantime the UK National Screening Committee [6] currently recommend against screening with PSA.

There is also no evidence to support digital rectal examination alone as a prostate screening tool in asymptomatic men[7].

Recommendations[8]:

- High risk patients ≥ 45 years old - Primary care health professionals can consider discussing prostate cancer risk and PSA testing when consulting with men with:
    - Black ethnicity
    - Family history of prostate cancer
    - Genetic risk factors such as BRCA gene variation that increase their risk

- Men ≥ 50 with no additional risk factors – should not be proactively invited for PSA testing but may request it. We should give men balanced information on pros and cons of the PSA blood test and diagnostic pathway and support them to make an informed choice on whether to have testing as per the prostate cancer risk management programme[9].

- Optimal intervals for repeat PSA testing in those without symptoms are unknown. Trials suggest this could be every 2 years for those at risk but could be every 8 years

for those at low risk with an initial PSA <1 aged 40 years or PSA <2 aged 60 years in those without a family history.

Men with symptoms[10,11]

Offer PSA testing to symptomatic men with:

- lower urinary tract symptoms scoring 8 or more on IPSS
- Erectile dysfunction
- Visible haematuria
- Prostate feels abnormal on digital rectal examination
- Unexplained weight loss
- Persistent bone pain

NICE suggests age-specific PSA thresholds for referral of:

40-49 years PSA > 2.5
50-59 years PSA > 3.5
60-69 years PSA > 4.5
70-79 years PSA > 6.5
Above 79: More than 10 and performance status 0-1, otherwise consider using advice and guidance or routine referral.

Additional things to remember when ordering and interpreting PSA tests

- PSA can be artificially high due to prostate inflammation, so ensure that a UTI is excluded and consider other causes (e.g. recent catheterisation, recent biopsy etc).
- Advise patient to avoid vigorous exercise and avoid ejaculation 48 hrs prior to testing.
- Digital rectal examination is not mandatory if PSA is raised but may be helpful in triaging referral.
- Consider repeat PSA after 6 weeks prior to referring if
    - PSA <10ng/ml and no risk factors
    - Recent urinary tract infection or instrumentation
- Finasteride and dutasteride reduce PSA levels by 50% - remember to multiply the result by 2 when considering referral thresholds.
- Men who have had prior treatment for prostate cancer may have a different PSA threshold. This should be determined by their urologist. If they are no longer under urological follow up and the threshold is unclear it would be sensible to clarify this using advice and guidance to urology.

PSA testing in men 80 years and above

NICE suggests we should use 'clinical judgement' when deciding whether to refer symptomatic men over 80 with an elevated PSA. Many cancers in this age group will be clinically insignificant and won't shorten life expectancy.

The Academy of Royal Colleges consensus on PSA testing for men over 80[12] states that treatments with an intention to cure a patient generally only have benefit if life expectancy

is >10 years. Men with asymptomatic prostate cancer aged over 80 are thought unlikely to benefit from hormonal manipulation in terms of quality of life versus medication side effects and so unless they have symptoms there is a rationale to avoid investigation or treatment.

Men with suspected metastatic disease should be referred to secondary care regardless of age as there are effective treatments which can manage the cancer and may improve symptoms.

Prostate cancer risk in transgender women[13]

The risk of prostate cancer in trangender women who are not on gender affirming hormone therapy or have not had gender affirming surgery is the same as the risk for cis men. However, awareness is low. The prostate is not removed as part of genital reconstructive surgery. Incidence in patients on gender affirming hormone therapy is lower but diagnosis and treatment can be more challenging.

Useful patient resources to aid decision making

- Prostate Cancer Risk Management Programme – PSA Testing and Prostate Cancer: Advice for men without symptoms
- NHS information 'Should I have a PSA test?'
- Prostate Cancer UK 'Are you at risk?' risk checker
- Cancer Matters Wessex – Prostate Cancer Campaign
- Risk calculators may be useful in helping people consider their risk factors e.g. Prostate Cancer Research Foundation Calculate your prostate cancer risk
- PCUK Information on risk for trans women https://prostatecanceruk.org/prostate-information-and-support/risk-and-symptoms/trans-women-and-prostate-cancer

References for health professionals

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