

The who, when and how of PSA testing

New Australian guidelines

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Recent consensus guidelines provide long-awaited clarity for GPs on how to approach PSA testing and interpret results.

When should you offer a prostate specific antigen (PSA) test to help determine a man's risk of prostate cancer? Should you even order a PSA test at all? The conflicting advice given to GPs has caused ongoing confusion for years.

Finally, however, Australian consensus guidelines – *Clinical Practice Guidelines for PSA Testing and Early Management of Test-Detected Prostate Cancer* – were published in January this year with the aim of putting an end to the confusion. This article gives an overview of the main points in these new guidelines on PSA testing.

The amount of controversy generated by the simple blood test for PSA has been no less than monumental.¹ Although the PSA level is principally used to stratify a man's risk of prostate cancer, we know that an abnormally elevated level occurs commonly in other conditions of the prostate, namely benign prostatic hyperplasia (BPH) and prostatitis. However, an elevated PSA level can lead to a string of invasive tests and treatments that may end up doing more harm than good to the man in question (who is now a patient).

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On the flipside, an elevated PSA level may be the first sign that a man is harbouring a prostate cancer that is still localised to the prostate, but that could spread and kill him if left untreated. And although it is true that most men with prostate cancer die with the disease rather than from it, it is important to remember that it is still the second most common cause of cancer-related death among men in Australia, behind lung cancer.²

PSA testing guidelines

Not surprisingly, these contrasting aspects of PSA testing have led to many different and changing guidelines that have further confused clinicians. However, earlier this year Australia achieved what is believed to be a world first: facilitated by Cancer Council Australia and the Prostate Cancer Foundation of Australia, an expert advisory panel that included GPs, epidemiologists, urologists, oncologists and public health experts published consensus guidelines for PSA testing.³

This is the first time experts from such a wide range of fields have reached consensus on this issue, and is therefore a remarkable achievement. Importantly, these evidence-based guidelines have gained NHMRC approval through a rigorous process and have been formally endorsed by the Royal Australian College of General Practitioners. So what do these new guidelines tell us?

Test the correct age group

Men aged from 50 to 69 years are considered the most appropriate for PSA testing because prostate cancer first becomes common among men in this age bracket. It is also an age at which the vast majority of men have a life expectancy of more than 15 years, so that if aggressive localised prostate cancer is present, there is a higher chance it will cause suffering in that man's expected lifetime, or even death, if it is left untreated.⁴ Unfortunately, statistics show that a large proportion of PSA testing occurs outside this age range, especially in men who are 70 years of age

1. KEY AUSTRALIAN GUIDELINE RECOMMENDATIONS FOR PSA TESTING

- The main target group for PSA testing is men who are 50 to 69 years of age
- Discuss the potential benefits and harms of PSA testing with men in this age group
- If a man wishes to have regular testing for prostate cancer, order a PSA test every two years
- A PSA level greater than 3.0 ng/mL is considered abnormal and warrants repeat PSA testing, including determination of a free-to-total PSA ratio, in one to three months' time
- Digital rectal examination is not recommended; however, it is an important part of assessment on referral to a urologist

and over,² without any evidence of benefit. Probably the biggest improvement we can make in PSA testing is simply to use it in the correct age group.

BPH is the most common cause of a slightly elevated PSA level,⁵ and commonly manifests in this same age group. Repeat PSA testing, including determination of a free-to-total PSA ratio, is required in patients with BPH to help rule out clinically significant cancer,⁶ which often occurs concurrently. Repeat testing is also required to rule out an aberrant elevation of PSA level, which is seen commonly on single testing (Box 1).

Inform men about the harms and benefits

Men need to know what they are facing before they decide to have a PSA test, and it is important they discuss the benefits and harms with their GP. If their PSA test result is abnormally high, they may require further tests such as a prostate biopsy, which carries its own risks, including sepsis, especially if performed transrectally.⁷ Then if significant cancer is found, they may need treatment, which may impact their quality of life through erectile dysfunction or urinary and bowel symptoms.

However, it is also important to stress that patients diagnosed with low-grade prostate cancer do not need treatment. Instead, active surveillance is most often indicated in patients with low-grade disease, allowing avoidance of unnecessary treatment while still keeping a watch to ensure the disease does not progress. In addition, recent advances in diagnostic methods used by urologists (such as multiparametric MRI and transperineal biopsy) can help to keep the risk of complications exceedingly low (see below).^{8,9}

The benefit of PSA testing is that it can enable detection of aggressive prostate cancer before it becomes incurable. The most rigorous evidence shows that PSA testing reduces both morbidity and mortality from prostate cancer.¹⁰

As even the more aggressive forms of prostate cancer are comparatively slow growing, annual PSA testing in patients

2. RECOMMENDED APPROACH TO PSA TESTING IN MEN WITH A FAMILY HISTORY OF PROSTATE CANCER

For men with increased risk of prostate cancer, such as having a father or brother diagnosed with prostate cancer before 60 years of age, offer an initial PSA at 40 to 45 years of age. Further testing is directed by the PSA level:

- If PSA level is less than 1.0 ng/mL, no further PSA testing is required until age 50 years
- If PSA level is 1.0 to 2.0 ng/mL, offer PSA testing every two years
- A PSA level greater than 2.0 ng/mL is considered abnormal and warrants repeat testing and determination of a free-to-total PSA ratio

whose previous levels were normal is not justified; however, evidence does support testing every second year.¹⁰

DRE is not mandatory

Digital rectal examination has not been recommended in the guidelines. It is an unpleasant experience that may deter men from having a check-up, and many GPs do not feel confident with their own findings. However, it is an important part of assessment on urologist referral as a small proportion of aggressive prostate cancers do not cause increased PSA levels. The Urological Society of Australia and New Zealand (USANZ) encourages GPs who feel confident in performing digital rectal examinations to continue to use the procedure.

When to refer

Although not specifically mentioned in the guidelines, men should be referred to a urologist when PSA levels remain abnormally elevated on repeat testing.

Men with a significant family history of prostate cancer are advised to start PSA testing earlier, at 40 to 45 years of age, as the chance of detecting significant cancer is higher in this younger age group. A sliding scale of PSA levels directs further testing and has 2.0 ng/mL as the lower cut-off for abnormal levels because BPH is rarely a confounder in younger men (Box 2).

Better accuracy and reduced risk in diagnosis

Noninvasive imaging, using multiparametric MRI, is revolutionising the way prostate cancer is diagnosed and managed. For the first time, prostate cancer can relatively reliably be seen on imaging, which enables urologists to target biopsies to suspicious areas. Furthermore, MRI typically only detects more aggressive cancers with a Gleason score of 7 and above, thus avoiding detection of indolent disease. However, the guidelines make the point that evidence does not yet support MRI for routine use prior to an initial biopsy. Instead it should be used

when suspicion of prostate cancer remains after a negative biopsy. In addition, until expertise in prostate MRI becomes widespread, MRI should only be ordered by urologists and performed by radiologists with appropriate training. Local data are needed to determine the utility of MRI in other settings.

In Australia and overseas there has also been a rapid increase in the use of transperineal biopsy. This approach avoids biopsy needle passage through the rectum, and as a result the rate of serious infection is exceedingly low. Transperineal biopsy also offers a fixed platform so the operator's hand is steadied, lending itself well to targeted biopsy of suspicious lesions seen on MRI. However, it typically requires a general anaesthetic and some centres may not have access to the required equipment. As such, the guidelines advise that transrectal biopsy is still acceptable.

Conclusion

The field of prostate cancer diagnostics is advancing at a rapid rate. But for now, it is hoped that having formulated these guidelines through consensus there can finally be some clarity for GPs on to whom, when and how to offer PSA testing. This achievement could provide an example to countries around the world and put an end to the confusion on PSA testing. **MT**

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