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PSA Testing for Prostate Cancer in Asymptomatic Men
Information for Health Practitioners

This information has been developed for health practitioners* to read before they discuss the prostate-specific antigen (PSA) test as part of a medical consultation. It provides a summary of the evidence on the benefits and harms of PSA testing, with or without digital rectal examination (DRE), for prostate cancer in asymptomatic men.

For the purposes of this document, asymptomatic men include those with stable lower urinary tract symptoms, because these symptoms are very common in ageing men and are not clearly associated with an increased risk for prostate cancer.

What are the potential benefits of PSA testing?

- ***Reassurance:*** If the PSA test result is normal or very low, this can provide reassurance.
- ***Early detection:*** If prostate cancer is detected at an early stage, when it is still confined to the prostate gland, there is an opportunity to commence early treatment.
- ***Early treatment:*** Early treatment may cure the disease, and thus avoid loss of quality of life due to advanced prostate cancer, and death from prostate cancer.

What are the potential harms of PSA testing?

- ***False positive results:*** If no cancer is present, a positive test may cause psychological distress and unnecessary prostate biopsies.
- ***False negative results:*** If prostate cancer is present, a normal or low PSA may provide false reassurance and may delay cancer diagnosis.
- ***Overdiagnosis:*** A positive PSA result may lead to diagnosis of a cancer that is progressing so slowly it would not have caused any health problems had it been left undetected and untreated.
- ***Overtreatment:*** Unnecessary treatment of slowly progressing cancer may result in harmful effects without any health benefit.

*This document is not a substitute for relevant clinical practice guidelines and therefore does not contain recommendations.

How frequent are these benefits and harms?

To help men make a decision, they should be informed of both the potential benefits and harms of PSA testing. These vary with age and familial risk. The following rates are *estimates* for men aged 60 years who have no first-degree relatives affected by prostate cancer and who, for the next 10 years, have an annual PSA test. Ideally, they would be based on current Australian active surveillance and treatment rates. However, since these figures are unavailable, the most recent relevant figures have been used, including evidence-based estimates of benefit.

Possible benefit of PSA testing

- For every 1000 men tested, 2 men will avoid death from prostate cancer before 85 years of age because of PSA testing[1]. This benefit might be greater for men at high risk of prostate cancer, such as those with a strong family history of the disease.
- For every 1000 men tested, 2 men will avoid metastatic prostate cancer before 85 years of age because of PSA testing[2].

Expected harms of PSA testing

False-positive results:

- For every 1000 men tested:
  - 87 men who do not have prostate cancer will have a false positive PSA test that will lead to a biopsy[1].
  - 28 men will experience a side effect from the biopsy that they consider to be a moderate/major problem that may require healthcare, and 1 will require hospitalisation[3].

Overdiagnosis:

- For every 1000 men tested, 28 men will have prostate cancer diagnosed as a result of the PSA test[1], many of whom would have remained asymptomatic for life (i.e. are overdiagnosed).

Overtreatment:

- For every 1000 men tested,
  - 25 men will choose to undergo treatment (surgery or radiation) because of uncertainty about which cancers need to be treated, many of whom would do well without treatment (i.e. are overtreated)[4].
  - 7–10 of these 25 men will develop persistent impotence and/or urinary incontinence, and some will develop persistent bowel problems, due to treatment[4].
- For every 2000 men tested, 1 man will experience a serious cardiovascular event, such as myocardial infarction, due to treatment[4].

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What research has been done to study the effectiveness of PSA testing for prostate cancer?

In 2013, the National Health and Medical Research Council (NHMRC) released an evaluation of the evidence on the effectiveness of prostate-specific antigen (PSA) testing of asymptomatic men in reducing mortality and morbidity from prostate cancer[5]. For the purposes of this evaluation, PSA testing refers to PSA testing with or without DRE.

The evaluation identified five relevant systematic reviews, which included a total of six randomised controlled trials (RCTs) of varying quality and with heterogeneous results that compared PSA testing (with or without DRE) with no PSA testing. These mass prostate cancer screening trials were conducted in North America and Europe. Participants ranged from 45 to 80 years, but most were aged between 50 to 74 years, with follow-up ranging from 6 to 14 years. This remains a short period relative to the natural history of prostate cancer. Trials ranged in size from 9000 to 182,000 men. Although some of these trials were well designed, they had some limitations that affect the interpretation of results. For example, in one trial, many men had a PSA test before they entered the trial, and in another, protocols varied between study centres[5].

Does PSA testing in asymptomatic men reduce their risk of dying from prostate cancer?

All six RCTs examined the effect of PSA testing on death from prostate cancer, but the findings were inconsistent. Of the two largest and most recent trials, one found that PSA testing led to a small but significant reduction in death from prostate cancer; the other found that PSA testing *did not* reduce death from prostate cancer. Thus, the present evidence is inconsistent as to whether PSA testing affects the risk of dying from prostate cancer.

Does PSA testing in asymptomatic men reduce their overall risk of dying?

Four RCTs, including the two largest trials, examined the effect of PSA testing on death from all causes. PSA testing appears to have no discernible effect on the overall risk of dying.

Does PSA testing in asymptomatic men reduce their risk of having metastases present at diagnosis of prostate cancer?

Four RCTs, including the two largest trials, examined the effect of PSA testing on the presence of prostate cancer metastases at diagnosis, most of which were in bone. There was some inconsistency in the definition of metastatic disease across the trials. However, overall, the evidence shows that PSA testing reduces the risk of having metastases present at diagnosis of prostate cancer. The largest RCT showed that after a median 12 years of follow up, the cumulative risk of prostate cancer metastases remained lower in those who had PSA testing than in those who did not.

Does PSA testing in asymptomatic men affect the quality of life of men who are diagnosed with prostate cancer?

None of the six RCTs has reported complete data on the effect of PSA testing on quality of life. Thus it is unknown whether PSA testing affects quality of life in the long term due to advanced prostate cancer. However, this uncertainty should be considered in the context of the potential benefits and harms outlined on the first page.

1. Howard K. et al., 'A Model of Prostate-Specific Antigen Screening Outcomes for Low- to High-Risk Men', *Arch Intern Med*, vol. 169, 2009, pp. 1603-1610.
2. National Health and Medical Research Council requested the calculation of this figure from Professor K. Howard, University of Sydney, using methods in Howard, K et al., *Arch Intern Med*, vol. 169, 2009, pp. 1603-1610 and results reported in Schroder, FH et al., *Eur Urol*, vol. 62, 2012, pp. 745–752.
3. Rosario DJ. et al. 'Short Term Outcomes of Prostate Biopsy in Men Tested for Cancer by Prostate Specific Antigen: Prospective Evaluation Within ProtecT Study', *BMJ*, vol. 344, 2012, pp. d7894.
4. Moyer VA. on behalf of the U.S. Preventive Services Task Force, 'Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement', *Ann Intern Med*, vol. 157, 2012, pp. 120–134.
5. National Health and Medical Research Council. Prostate-Specific Antigen (PSA) testing in asymptomatic men: Evidence Evaluation Report. Commonwealth of Australia, 2013. Available at: http://www.nhmrc.gov.au/guidelines/publications/men4

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This information has been developed for health practitioners*, to support discussion with men and their families about the benefits and harms of prostate-specific antigen (PSA) testing for prostate cancer.

Frequently asked questions about PSA testing for prostate cancer

Why is prostate cancer important?

Prostate cancer is the most commonly diagnosed cancer in Australia and second most common cause of male cancer deaths[1]. Both the risk of developing prostate cancer and the risk of dying from prostate cancer increase considerably from age 50 to 70 years (Table 1). Men with a family history of prostate cancer are also at higher risk of developing prostate cancer.

What is a PSA test?

A PSA test is a blood test that is commonly used to detect possible prostate cancer. It involves taking a sample of blood to measure the concentration of PSA, a protein produced by cells in the prostate gland. Elevated PSA levels may indicate the presence of prostate cancer, but may also be caused by other conditions, such as benign prostate enlargement or a prostatic infection.

How accurate is a PSA test?

A PSA test is used to evaluate the probability that prostate cancer is present – it does not diagnose prostate cancer. A prostate biopsy is the only method by which prostate cancer can be definitively diagnosed.

The PSA test is not perfect:

- For every 10 men who have an abnormal PSA test result, about 7 will not be diagnosed with prostate cancer after further diagnostic evaluation; that is, the result is a false positive.
- A small proportion of men with a normal PSA test result will have prostate cancer; that is, the result is a false negative.

Many prostate cancers found by PSA testing are slow-growing and thus not life-threatening, so they may not cause a man any harm during his lifetime. PSA testing does not accurately determine which cancers are likely to be a threat to a man's health and which are not.

Are there any other tests available for prostate cancer?

There are other tests, such as free PSA, Prostate Health Index (PHI), PCA3 urine test and multi-parametric magnetic resonance imaging (MRI), but these either have not been shown to be superior to PSA alone or are yet to be fully evaluated. Digital rectal examination (DRE) is also used with the PSA test to test for prostate cancer.

Table 1: Age-specific risks of diagnosis and death from prostate cancer

	Within the next 10 years		Within the next 20 years	
For a man currently aged	What is the chance of a diagnosis of prostate cancer?[a]	What is the chance of dying from prostate cancer?[b]	What is the chance of a diagnosis of prostate cancer?[a]	What is the chance of dying from prostate cancer?[b]
40 years	*4 in 1000*	*0 in 1000*	*33 in 1000*	*1 in 1000*
50 years	*30 in 1000*	*1 in 1000*	*109 in 1000*	*4 in 1000*
60 years	*82 in 1000*	*4 in 1000*	*172 in 1000*	*19 in 1000*
70 years	*98 in 1000*	*15 in 1000*	*176 in 1000*	*69 in 1000*

Sources:

a) Australian Cancer Database 2010, Australian Institute of Health and Welfare (AIHW). Based on the most recent complete national incidence data available (2009).

b) Analysis of AIHW National Mortality Database, based on the most recent national mortality data available (2011). The mortality data in the AIHW National Mortality Database were provided by the Registries of Births, Deaths and Marriages and the National Coronial Information System and coded by the Australian Bureau of Statistics

*This document is not a substitute for relevant clinical practice guidelines and therefore does not contain recommendations.

1. Australian Institute of Health and Welfare (AIHW) 2013. Prostate cancer in Australia. Cancer series no. 79. Cat. no. CAN 76. Canberra: AIHW.

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How can men prepare for a PSA test?

Men should not have a PSA test if they have:

- an active urinary infection;
- ejaculated in the last 48 hours;
- exercised vigorously in the last 48 hours;
- had a prostate biopsy in the last 6 weeks; or
- had a DRE in the past week.

Any one of these can cause an elevation of PSA levels.

What are considered normal and abnormal PSA test results?

PSA levels increase as men age. Therefore, an age-specific reference range should be used when deciding whether the test results are normal or abnormal. Repeat tests should be done by the same laboratory.

What happens if a man receives a normal PSA test result?

A normal PSA test result indicates that prostate cancer is unlikely to be present. No further action may be needed. If the PSA level is at the upper end of the reference range and/or if there is a family history of prostate cancer, the test may be repeated.

A normal PSA test result may alleviate anxiety but does not guarantee that no cancer is present. If a man has a normal test result but wishes to continue to be tested for prostate cancer, he may consider having another PSA test in a year or two. Some doctors may suggest a time to the next PSA test, based on the current test result.

What happens if a man receives an abnormal PSA test result?

An abnormal PSA test result should not be ignored. It can cause worry and anxiety because it indicates the possible presence of prostate cancer; however, it does not confirm that cancer is present. Usually, an abnormal PSA test will be repeated. If the result remains abnormal, a man may choose to be referred to a specialist for further investigations. If the PSA level is rising, the specialist may recommend a prostate biopsy, which can diagnose prostate cancer early when a cure may be possible. However, as with the PSA test, the biopsy is not a perfect test:

- If the biopsy is negative, further follow-up or monitoring may still be necessary.
- The biopsy may cause embarrassment, anxiety and discomfort.
- The biopsy may lead to complications, such as blood in the urine or semen, or infection.
- Some men experience pain from the biopsy, although this can be reduced by local anaesthetics or sedation.

If a man receives a diagnosis of prostate cancer after an abnormal PSA test, what choices does he have?

Not all prostate cancers require treatment. If a man is diagnosed with prostate cancer, the options depend on the stage and grade of the cancer. A positive biopsy does not necessarily indicate that the cancer will cause harm if left untreated.

Observation

Watchful waiting is an approach to management of the disease usually in older men with limited life expectancies. *Active surveillance* is an active plan to postpone intervention, in which men are closely monitored for signs of disease progression. The practitioner will recommend treatment with palliative intent if the disease progresses.

Active treatment

In men who require treatment with curative intent, the choices include radical prostatectomy, radiation therapy and, for locally advanced or metastatic disease, androgen deprivation therapy. The possible side effects of treatments vary and can have a negative effect on quality of life. Known side effects include urinary incontinence, impotence, bowel dysfunction, and complications immediately after surgery. Men should be encouraged to discuss management options with their general practitioner and specialist.

If a man decides not to have a PSA test what risks should he and his family be aware of?

Deciding not to have a PSA test is appropriate for many men. In the unlikely event that a man who decides not to have a PSA test has a potentially fatal prostate cancer, he may miss the opportunity for early detection and early treatment. If prostate cancer is not diagnosed and treated until it causes symptoms, such as blood in the urine or bone pain, it may have spread beyond the prostate and be incurable. Symptom management may include androgen deprivation therapy, radiotherapy and chemotherapy amongst others.

References

Australian Institute of Health and Welfare (AIHW) 2013. Prostate cancer in Australia. Cancer series no. 79. Cat. no. CAN 76. Canberra: AIHW

Australian Institute of Health and Welfare (AIHW) National Mortality Database.

Howard K. et al., 'A Model of Prostate-Specific Antigen Screening Outcomes for Low- to High-Risk Men', *Arch Intern Med,* vol. 169, 2009, pp. 1603-1610.

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Rosario DJ. et al., 'Short Term Outcomes of Prostate Biopsy in Men Tested for Cancer by Prostate Specific Antigen: Prospective Evaluation Within ProtecT Study', *BMJ,* vol. 344, 2012, pp. d7894