
# The PSA debate

## Prostate cancer[1]

Routine screening for prostate cancer with digital rectal examination (DRE), serum tumour markers or transabdominal ultrasound is not recommended **(D)**.

| Question | Answer | Level of evidence and strength of recommendation |
|---|---|---|
| Should there be screening? | Currently no evidence that mass screening reduces mortality. | V–D |
| Is there any benefit in using a case finding (opportunistic medical screening) approach? | There is no demonstrable benefit. | III–D |
| Are PSA or DRE suitable for screening for prostate cancer? | PSA is unsuitable for screening because of low positive predictive value and known risks or adverse effects of therapies that have unknown effectiveness. DRE is not recommended. | V–D |

### Reference

1. Australian Family Physician. Guidelines for preventive activities in general practice. 5th edn. Melbourne: RACGP, 2001; 30(Special issue):S36–S37.

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## Current studies

There is currently a Cochrane group systematically reviewing trials of the effectiveness of prostate screening.[1] However, systematic reviews of research conducted to date fail to demonstrate the effectiveness current screening.[2] This is for a number of reasons. First, the uncertain effectiveness of aggressive treatment for prostate cancer and a reservoir of unsuspected indolent cancers make prostate cancer ill-suited for screening especially if there are significant numbers of false positive screening tests putting patients at risk for subsequent investigations.[3] Second, the prostate specific antigen (PSA) test and follow up biopsies cannot reliably predict if a man has cancer that will progress to cause illness or death. There are a large proportion of men with unsuspected prostate cancers that may not cause morbidity or mortality and are unlikely to benefit from aggressive treatment. Finally, there have been no studies that have demonstrated that prostate cancer screening reduces mortality.

### References

1. Bonfill X, Dalmau-Matarrodona E, Wilt T. Screening for prostatic cancer: protocol. Cochrane Database, 2000.
2. Database of abstracts of reviews of effectiveness. Screening for prostate cancer. 4 December 2002.
3. Godley P. Prostate cancer screening: promise and peril: A review. Cancer Detect Prev 1999; 23(4):316–324.

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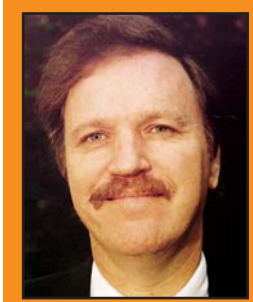
**Mark Harris**



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## PSA testing

Prostate specific antigen (PSA) screening, particularly when combined with rectal examination, is considered to be a valid means of diagnosing prostate cancer. However, test results can be unreliable and it is yet to be proven absolutely that PSA based prostate cancer screening actually helps reduce mortality rates.

Therefore, it is the opinion of most cancer societies around the world and the Urological Society of Australasia that mass population screening cannot be justified.

However, it is recommended that men in susceptible age groups should be made aware of the test and given sufficient information about its benefits and risks, so that an informed decision whether to test or not to test can be made. There is now ample evidence from databases in the USA to suggest that PSA testing has increased detection of localised cancers that are pathologically significant. There also appears to be a decreased risk of metastatic cancer or cancer spread in patients whose cancer has been detected through PSA screening.

Preliminary research also suggests that death rates from prostate cancer have dropped in geographic areas that have adopted a mass screening policy. A recent study from the Federal State of Tyrol in Austria which introduced mass screening as compared to the rest of Austria which did not, noted a 45% difference in prostate cancer mortality suggesting a benefit from PSA screening and early detection and treatment.[1]

Mortality worldwide from prostate cancer has fallen by 20% in recent years and while other explanations are possible, such as the earlier use of hormone therapy, it is certainly plausible that the drop may be due to the early detection and treatment of prostate cancer.

Furthermore a review of cut off levels for PSA that are currently set at 4 ng/mL is recommended. It is clear that significant prostate cancer exists with PSA levels between 2.5 ng/mL and 4 ng/mL. As such, it would seem that refining PSA levels and defining clearer testing intervals would be appropriate as future research needs.

### Reference

1. Bartsch G, Horninger W, Klocker H, et al. The Tyrol Prostate Cancer Screening Group. Prostate cancer mortality after introduction of prostate specific antigen mass screening in the Federal State of Tyrol, Austria. Urology 2001; 58:417–424.



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## Contemporary view of prostate cancer diagnosis and treatment

There is no dispute that at the present time, based on levels of evidence, there is not yet conclusive proof that mass screening of the population for prostate cancer using PSA testing can be justified. However, men with a family history of prostate cancer should be tested annually from the age of 40 years.

In early prostate cancer there have been substantial changes in clinical expression, and rational approach to delivery of therapy, and improvement in hormone therapy for advanced prostate cancer. There are some widely held erroneous views regarding prostate cancer, particularly relating to incidental disease and translating that to a more general view that prostate cancer is symbiotic and not harmful to the patient. We should ask the following questions.

### Incidental or autopsy found latent prostate cancer?

Prostate cancer has a complex natural history and there is a very high prevalence of incidence over clinically expressed prostate cancer. There is a high prevalence of subclinical or preneoplastic latent prostate cancer. Latent prostate cancer is found in 30% of men less than 50 years of age.[1] Autopsy studies have shown these men have subclinical foci of prostate cancer. This is universal and there is no geographic or ethnic variation in incidence. Latent prostate cancer, or subclinical prostate cancer is not detected by PSA. Latent prostate cancer, ie. cancer with a Gleason score less than six and a volume less than 0.5 cc, is only diagnosed in screening programs at a rate between 3% and 16%. Prostate specific antigen does not rise when the bulk of prostate cancer is less than 0.5 cc.

### Does PSA diagnosed prostate cancer offer a lead time to allow potentially curative therapy?

The Physicians Health Study showed that PSA diagnosed prostate cancer allows a lead time of 5.5 years in the diagnosis of lethal prostate cancer.[2] There has been a 50% drop in the rate of newly diagnosed prostate cancer which is metastatic. We are seeing an earlier stage diagnosis in young men

and an increased rate of organ confined, potentially curable, cancer. Organ confined prostate cancer can be treated with curative intent by surgery or radiation therapy. A recent study in the British Journal of Urology[3] concluded that PSA detected prostate cancer allows a mean of nine years before clinical presentation. Once prostate cancer is symptomatic, ie. metastatic death ensues between 2–3 years. Before the PSA era few men examined for prostate cancer who were found to have abnormal digital rectal examination were diagnosed with early prostate cancer.

### Is histological prostate cancer lethal if untreated?

There are numerous studies showing that well differentiated prostate cancer does not bring about the death of the host, whereas moderate to poorly differentiated prostate cancer, ie. a Gleason score of 6, 7 and beyond, will kill a host if untreated.[4] A majority of patients presenting for curative therapy, ie. PSA detected T1C prostate cancer have a Gleason score of 6, 7 or beyond.

Lu-Yao[5] reported on 60 000 patients stratified by their Gleason score from 2–10 and who were treated by surgery, radiation or watchful waiting. Those men with high grade prostate cancer died in large numbers without treatment. Patients with a Gleason score of 8 or beyond treated with watchful waiting had a 45% cancer specific survival. Those treated with surgery had a 67% prostate cancer survival, ie. a 50% improvement in survival.

### Do modern curative therapies offer a real cure?

A number of studies have attested to the ability of surgery or radiation therapy to cure high grade organ confined prostate cancer. Catalona[6] reported 10 year survival rates for men treated with radical prostatectomy for organ confined high grade prostate cancer of 80%, and 71% at 15 years for men with Gleason grade 7 cancers and above.[6]

Data from modern surgical series clearly support the concept that cure is possible for men with prostate cancer which untreated would kill the individual. It appears that we can offer curative therapy to those who truly need it.

Albertson[5] has shown that watchful waiting for men with high grade prostate cancer, ie. a Gleason score of 7 and above, will bring about the death of that patient within 10 years.

We are seeing both a reduction in the number of men presenting with metastatic disease and an increase in the number of men being treated with organ confined disease for cure. To justify the offer of curative therapy by surgery or radiation therapy a patient needs to have a life expectancy of 10 years.

### Are we seeing a reduction in prostate cancer mortality?

A recent study published by Chu et al[7] stated prostate cancer mortality showed a transient increase in the USA after 1986 when the USA FDA approved the use of PSA testing. The age adjusted prostate cancer mortality rates for men aged 50–84 years however, have dropped below the 1986 rate since 1995 for white men, and 1997 for black men. In fact, for men aged between 50–79 years the 1998 and 1999 rates were the lowest prostate cancer mortality observed since 1950. Mortality rates by disease stage show a decline in death from metastatic disease and not because of improved treatment of men with metastatic prostate cancer. Increased detection of prostate cancer before it becomes metastatic, possibly reflecting increased use of PSA testing after 1986, may explain much of the recent mortality decrease in both white and black men.

In figures released by the New South Wales Cancer Registry up to the year 2000, the prostate cancer mortality made a clear decline from the years 1993 through to 2000. In Australia where routine PSA testing is not recommended, but widely practised, significant decrease in mortality from prostate cancer is being observed.

## Conclusion

It is time to move on from the unanswerable debate regarding prostate cancer population screening to discuss the above questions and discuss a new paradigm. The morbidity of current curative therapy is still unacceptable although there have been dramatic improvements in reduction of morbidity in these therapies. The new field of proteomics will almost certainly lead to the development of new highly sensitive and specific markers for prostate cancer and be able to differentiate between incidental and lethal prostate cancer.

### References

1. Sakrwa, Grignondj, Haas G P. Pathology of premalignant lesions and carcinoma of prostate in African American men. Semin Urol Oncol 1998; 16:214–220.

2. Roberts R O, et al. 1999 Decline in prostate cancer mortality from 1980-1997 and an update on incident trends In Minicota. J Urol 1999; 161(2):529–533.
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4. Albertson P C, Hanley J A, Gleason D F, Barry M J. Competing risk analysis of men aged 55-74 years at diagnosis managed conservatively for clinically localised prostate cancer. JAMA 1998; 280:975–980.
5. Lu-Yao G L. Population based study of long term survival in patients with clinically localised prostate cancer. Lancet 1997; 349:906–910.
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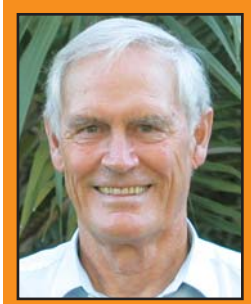
# Testing for prostate cancer

## A consumer view

**Max Gardner**



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The only advantage of being diagnosed with prostate cancer is being forced to become familiar with the intricacies of this controversial disease. There is a large body of real life experience among 'consumers' that should be of interest to practitioners as they struggle with the issues prostate cancer presents.

Controversy surrounds the issue of routine PSA testing. Many prostate cancer specialists believe the weight of evidence is moving strongly in favour of testing, early detection and treatment. In the past decade, the death rates from prostate cancer have decreased in every country in which PSA testing has been introduced, including Australia.

Today, the reality is that any Australian man of appropriate age wishing to have a PSA test is entitled to have one each year on Medicare. If the test suggests the presence of prostate cancer, the patient will be examined by specialists and, if disease is confirmed, offered appropriate treatment. Whatever the downside of testing and treatment, the fact is that most prostate cancer specialists recommend testing.

If specialists in prostate cancer recommend that men be tested for prostate cancer by the PSA test, yet other opinion leaders state that the benefits of mass PSA screening are not yet proven, where does that leave general practitioners?

The problem for GPs is that they are the gatekeepers to the PSA test. They cannot avoid the controversy. How should they respond to an asymptomatic man who asks about being tested? Should they advise for or against testing? Under the time constraints of clinical practice, how can they possibly explain the intricacies of testing for prostate cancer to a man who will almost certainly have no knowledge of such matters? Is their own knowledge sufficient to allow them to explain the issues? What about legal liability? This is potentially dangerous ground for GPs.

Perhaps the experience of men who have faced diagnosis and treatment for the disease might be helpful. We believe the issue is beyond dispute. Only men themselves should decide whether to be tested. But before men can make an informed decision, they and their families need a program of public education to fully inform them of the risks they may face from prostate cancer. They need to understand the benefits and implications of being tested.

### What consumers need to know

At diagnosis, most men are unaware they have a prostate, where it is located or what role it performs; let alone that it could become cancerous and threaten their lives. Compare that with the state of women's awareness of breast and gynecological cancers. This difference in awareness is at the heart of the problem with prostate cancer. The idea that GPs can be expected to educate the entire male population on prostate cancer is simply ludicrous. At the very least, a sustained public education campaign is needed.

When men are made aware of the disease, they must be informed that a simple PSA blood test is available. However, they should also understand that if the test shows an elevated PSA, further testing may be needed to determine if prostate cancer is present.

Men need to know that prostate cancer in its curable stage seldom has symptoms. To reduce the risk of death, they must detect and treat the disease early, while it is still confined to the prostate. At present, only PSA testing is likely to detect the disease early enough for cure. Waiting for symptoms is simply tempting fate.

Men need to be aware that, over an average

lifetime, their risk of experiencing prostate cancer is one in 10. Put another way, men have a nine out of 10 chance they will never develop prostate cancer. If the risk of one in 10 seems enough to encourage men to be tested, they should know the greatest benefit will accrue between 50–70 years of age. Testing before or after this age is not likely to be effective, except in cases of family history of the disease, where testing should commence at 40 years of age. However, if testing occurs every two years, developing prostate cancer should be detected in time for curative treatment.

Much is made of the 'harms' of being treated, particularly impotence and incontinence, however, recently improved techniques have reduced unwanted side effects. However, men who have been diagnosed and treated consider such side effects as modest compared to having to endure extended treatment and probable death from advanced prostate cancer. They also recognise that advanced disease will inevitably be accompanied by incontinence and impotence, as well as excruciatingly painful bony metastases and other horrors.

Consumers believe that men need to be fully informed on all the above points. Only then will men be in a position to assess their risk from prostate cancer properly and make their own decision on whether to be tested.

In my view, that decision lies with men themselves, not with the medical profession or bureaucracy. However, the responsibility for informing men fully clearly lies with the community, as it already does with breast and gynecological cancers.

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## Medicolegal issues

**Paul Nisselle**

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Mass population screening for prostate cancer remains a controversial topic. It is not yet proven that mass screening, say, of all men over 50 years of age, reduces prostate cancer mortality. Opponents of screening say there is considerable morbidity associated with screening because the relatively high number of false positive PSA tests leads to many men being unnecessarily exposed to the complications of prostate biopsies. Supporters, while acknowledging that the jury is still out on the question of whether earlier detection and earlier radical treatment of prostate cancer reduces mortality, say there are good theoretical grounds for thinking that it does; enough that men should be advised individually of the risks and possible benefits of prostate cancer screening by digital rectal examination and PSA testing, thus enabling them to make their own informed choice whether or not to proceed. Put that way, both arguments are correct. Screening by PSA testing does lead to a need to perform a large number of what are ultimately shown to be unnecessary prostate biopsies. Similarly, it would seem consistent with treatment of cancer generally to predict that early detection and radical treatment of local lesions will improve cure rates.

The medicolegal issue is not based on the best interests of the community but what information and advice you give or should give to each man over the age of 50 who enters your consulting room. It is not the doctor's duty to decide whether or not, in an individual case, the patient should be screened. I think, and it is a personal view, that the current controversy suggests a need to inform men over 50 years of age about:

- screening for prostate cancer
- what screening entails
- what might be the consequences of screening, and
- what might be the consequences of not being screened;

stressing that PSA testing is a controversial issue. Patients often ask: 'What would you do if you were me, doc?' I think doctors should be careful how they answer that question, because while the patient is entitled to an honest answer, you want to be careful you do not dissuade them from making their own decision by giving them the 'easy' option of just doing what you implicitly advise by indicating your view.

In short, I think in the current climate, doctors should initiate provision of information about prostate screening to any man over the age of 50 years, and respect the patient's right to make his own informed decision whether or not to proceed.

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