



Screening for Prostate Cancer

It is now clear that screening for Prostate Cancer discovers the disease at an earlier and more curable stage. It is not yet clear whether this translates into reduced mortality from prostate cancer. The matter remains controversial both among urologists and epidemiologists. The Urological Society of Australasia believes that men in the 50-70 year age group with at least a 10 year life-expectancy, should be able to be screened, after appropriate counselling regarding the potential risks and benefits.

The Patients Guide to Screening for Prostate Cancer

Currently, doctors have varied opinions about whether men without symptoms should be tested (screened) for prostate cancer. Screening has both advantages and potential disadvantages. Until further studies are completed, patients should decide for themselves if they wish to be tested. This information is intended to help in making that decision. You should discuss any questions that you have, with your doctor.

Advantages of Screening

Prostate Cancer is common, and caused 2500 deaths in Australia in 1995. Advanced prostate cancer is not curable. In the absence of screening, only a low percentage of men are diagnosed with early-stage disease that is potentially curable. Screening discovers more cases of prostate cancer, and they are usually at an earlier stage at diagnosis. Prostate Cancer is often slow growing, and there is often a period after early detection when the cancer remains confined to the prostate. Several treatments are available that may cure prostate cancer if it is confined to the prostate. Screening is the probably the best way to minimise the risk of death from prostate cancer. Some men find a negative screening result reassuring, and it may reduce anxiety.

Disadvantages of Screening

No study has yet proven that screening reduces mortality from prostate cancer.

Many men with prostate cancer will die from other causes before suffering from advanced prostate cancer. Men who die from prostate cancer are often elderly.

Only 9% are under 65, and 62% of them are over 75. Screening is not always accurate. Some cancers may be missed, and many men with a raised (positive) screening test will NOT have cancer.

Though the first screen is only a blood test and a rectal examination, further testing (biopsy) may be necessary in 15% of men. 80% of those requiring biopsy will NOT have cancer, and therefore suffer some anxiety and risk without cancer being present.

It is difficult to predict which cancers may progress and which are incidental, or unlikely to limit the man's life. Treatments for prostate cancer all have side effects, often including some risks to erections and urinary control.

NOT screening is the best way to maximise a man's quality of life, because there is less risk of treatment side effects. It will also avoid the anxiety of the testing process

Screening is most likely to be beneficial in men between 50-70 years of age, as long their general health is otherwise good ie they have at least a 10-year life expectancy. If there is a family history of prostate cancer in either father or brother, (especially if diagnosed at less than 55 years of age) then screening may have an added benefit. In some men screening may be appropriate from 40 or 45, but the benefits of screening in most men <50 or >70 are lessened.



The decision about screening depends on each individual's goals, fears, and willingness to accept risks. Screening should be performed if the man wishes to maximise his lifespan and minimise his risk of dying from prostate cancer. Screening should not be performed if the man wishes to maximise his quality of life, minimise his risk of complications, and have only those medical tests that have clearly been proven to be beneficial.

Criteria for screening

Screening is the process by which asymptomatic people are tested to determine whether they are likely to have a particular disease. The sole aim is to detect and treat the disease at an earlier stage than if it was detected after symptoms occurred. The screening process is deemed successful if the tested population has increased longevity (due to lower disease-specific mortality) when compared with a control population.

The accepted criteria for screening for any specific disease are

1. Known natural history of the disease
 - High prevalence
 - Significant resultant mortality
 - Recognisable latent phase
2. Suitable screening test available
 - High specificity and sensitivity
 - Low or acceptable morbidity of screening
 - Low cost
3. Available treatments of proven benefit
 - Lead to increased longevity
 - Acceptably low morbidity
4. Costs acceptable to the Community
 - of case finding, diagnosis and treatment.

Official attitudes to screening

Major medical groups have varied attitudes to screening for prostate cancer, and this is reflected in recent editorial reviews in the major Journals. The American Urological Association supports community screening ie. screening of asymptomatic men of men in the 50-70 year age group without counselling. The American Cancer Society revised its guidelines in 1997 to advise screening with similar guidelines to those recommended by the Urological Society of Australasia (see box). However the US Preventative Services Task Force, the Canadian T. F. Periodic Health Exam and the UK Health Care Evaluation Unit all advise against screening. In Australia, the Australian Cancer Society and the Australian Health Technology Advisory Panel found screening for Prostate Cancer to be of unproven benefit. As a result of these reviews, the RACGP does not currently recommend community screening without informed consent. There are good reasons for these differences in official guidelines, yet men should have access to the facts to make an informed individual decision, since screening would almost certainly reduce their risk of dying from prostate cancer. It must be an individual's decision (aided by his doctor) whether he wishes to accept the risks of the screening process, in order to pursue the possible gains of increased longevity.

Position of the Urological Society of Australia and New Zealand

Population screening of asymptomatic men is not recommended. Individual men in the age group 50-70 with at least a 10 year life-expectancy (or men >40 with a strong family history) should be able to undertake screening by annual DRE and PSA testing, after appropriate counselling regarding the potential risks and benefits of investigations, and the controversies of treatment. It should be left to the individual doctor to decide whether to advocate testing in a man not requesting it.



Epidemiology

Prostate Cancer is now the most common cancer diagnosed in men, apart from non-melanotic skin cancer. The incidence has risen rapidly since 1990 when PSA testing became widely available. The graph provided by the Anti-Cancer Council of Victoria clearly illustrates this rise, and also shows the contrasting minor increase in age-adjusted mortality over the period 1982-1995. It is assumed that disease prevalence is unchanged and that the increase in incidence is a direct outcome of screening in the community. Proponents of screening will argue that this initial increase in cases diagnosed is to be expected, and the effects of reduction in mortality would take some 10-15 years to become apparent.

Many men diagnosed with prostate cancer do not die from the disease. Different studies offer varied opinions and it obviously depends on the stage and grade of the disease at diagnosis. The latest figures available in Australia show 2564 deaths due to prostate cancer in 1995, and 11,994 cases diagnosed in that year. Table 1 shows the interesting contrasts of the figures for men diagnosed with Prostate, Colo-rectal and Lung cancer. Though twice as many cases of prostate cancer were discovered compared with lung cancer, the latter caused almost twice the number of deaths. For contrast, the comparative numbers are listed for breast cancer in women.

Higher risk groups

Family History. A man's relative risk of developing prostate cancer is 2 or 3 fold higher if he has a first degree relative with prostate cancer. The genetic inheritance risk appears higher in families with men who develop prostate cancer before the age of 55, and others may have a sporadic form of the disease. Work is in progress to define the genetic abnormalities in the hereditary group, and this may provide a group of men who should have screening commenced at a younger age. At this time, it is recommended that men with a father or brother who had prostate cancer diagnosed before 55 should consider annual screening from 40years of age onwards. (Selective screening)

Racial Variations. African-Americans have a higher risk of death from prostate cancer, and Asian men a lower risk. These variations can be considered in decisions about screening of individuals, and of various communities.

Screening tests available

The combination of Digital rectal examination of the prostate (DRE) and measurement of the blood level of Prostate Specific Antigen (PSA) offers a reasonable sensitivity for detection of prostate cancer, but the specificity is relatively poor. The commonly quoted range for normal PSA is 0-4ng/ml. In the range 4-10, only 25% of men will have cancer detected on biopsy. The PSA level can rise due to Benign Prostatic Hyperplasia or prostatitis or instrumentation, and it must be clear that PSA is Prostate Specific, but not Cancer Specific. If the PSA is over 10, >50% of men will have cancer. With regard to sensitivity, 25% of men whose PSA is <4 will still have cancer. An abnormal area of hardness palpable on DRE would detect some of these cancers, so it is important that men requesting screening have both a PSA and Rectal exam.

Efforts have been made to improve the accuracy of screening, and this may help to reduce the number of unnecessary biopsies, and the resultant anxiety for men who test positive to initial screening but do not have cancer detected.

PSA Velocity measures the rate of change in PSA over time. A steadily rising PSA was thought to indicate a higher risk of cancer, and perhaps may be of help in men with PSA levels in the 4-10 range. However recent studies have shown PSA variations of up to 20% in consecutive daily measurements, so PSA velocity is not yet of proven value.



PSA Density rates the PSA level against the volume of the prostate as measured by trans-rectal ultrasound. Since large benign glands cause a rise in PSA, it was hoped that adjustment for prostatic volume would improve specificity, but this has not been confirmed. It may still be help in assessment of those men with a raised PSA but previously negative biopsy.

Age-related PSA is sometimes used to adjust for the natural increase in BPH with age, and the resultant PSA rise. Levels for those over 70 or 75 are therefore higher, but few groups recommend screening of men over 70. This relates to their other competing risks, and reduced remaining lifespan. In men under 60, some proposed a lower cutoff in PSA with consideration of biopsy for PSA levels of >2.5 or 3. This aimed to reduce the numbers of localised cancers being missed, but will necessarily increase the numbers of men requiring biopsy. It has not been universally adapted.

% Free PSA. The majority of PSA is bound to alpha-1-antichymotrypsin. For unclear reasons, men with BPH have a higher proportion of PSA that is unbound (%Free PSA) than do men with cancer. PSA measurement techniques previously measured both free and bound PSA, but it is now possible to measure both components separately. Patients with a %Free PSA less than 20%, have a higher risk of cancer. This may enable some men to avoid unnecessary biopsy, but may risk a small number of cancers being missed.

Neural Networks. There is a commercially available index (Prostasure*) which derives from calculations including the PSA level, Prostatic Acid Phosphatase, Creatinine phosphokinase enzymes, and the man's age. Though this has been publicised in some areas in Australia, the published data is preliminary and only applicable to PSA levels in the 4-10 range. The test is unproven in the Australian population.

Outcomes of screening

A screening of 100 men in the 50-70 year age group would result in approximately 15% having an elevated PSA or abnormal DRE. Follow-up biopsy under trans-rectal ultrasound control (TRUS) would be necessary to confirm or exclude cancer. These biopsies are uncomfortable but usually not painful. They have a risk of sepsis in 1-3% of cases, and significant bleeding in 1%. When TRUS was first introduced, it was suggested that the ultrasound appearance could be characteristic for cancer. Most urologists no longer believe this, and TRUS alone without biopsy is not an appropriate screening method.

While waiting for the biopsy results, there is inevitably some anxiety, as with other screening tests (eg breast biopsy) and this is concerning in the many men who have a raised PSA but no cancer present.

Should cancer be discovered, the man must then consider the treatment options, and the various side effects. There remains much conjecture about the advantages of surgery (radical prostatectomy), radiotherapy, brachytherapy, hormonal therapy or a program of watchful waiting. There is no randomised-controlled trial currently available to prove a survival advantage of any one choice, though there are individual case series with good results in selected patient groups. All of the therapeutic options carry the risk of side effects, with the risk of a degree of impotence or incontinence a concern to men who usually had no symptoms at the time of initial screening.

Prior to the introduction of PSA testing, many men who presented with prostate cancer had advanced metastatic disease. The percentage of men with disease confined to the prostate is certainly greater in a screened population, and the potential for curative surgery is therefore higher. Nevertheless, not all cancers found by screening are cured, and the morbidity of treatment remains significant.



Evidence for effectiveness of screening

There is increasing evidence that screening for prostate cancer has achieved:

A lower stage at first diagnosis.

Less metastatic disease and more cancers confined to the prostate margins at surgery.

A lower grade at first diagnosis.

Initial increased numbers of cancers being diagnosed. In some communities this has now started to drop, either due to reduced numbers of undetected cancers ("the cull affect") or possibly due to a drift away from screening.

Possible change in mortality. In the USA there has recently been a reduction in mortality from prostate cancer for the first time for some years. However it is not yet proven if this is a result of screening.

Difficulties in assessing screening programs

Lead Time Bias. Earlier diagnosis in the screened population is evident in the above evidence. This may produce an apparent improvement in results, with longer survival times when measured from the time of first diagnosis. This may not be necessarily be a result of postponement of the date of death, but may be due to advancement of the date of diagnosis.

Length time Bias. An annual screening program will tend to pick up slower growing cancers, and aggressive cancers will have a lesser possibility of discovery. Results of the treatment of such lower grade cancers would appear better. Unfortunately it is the aggressive cancers that will be life threatening.

Overdiagnosis Bias. A screening program may discover greater numbers of "incidental" cancers, which may not have been a limitation to longevity. Proponents of screening argue that the majority of cancers diagnosed are larger and of higher grade than "autopsy incidental" cancers.

Volunteer Bias. Is the screened group typical of the community? Most screening programs attract men who are more likely to be careful about their health and may therefore be at lower risk of death from other causes.

Informed consent

General Practitioners are those usually confronted with the issues of a man's initial decision. It may be helpful to use some written material about the pros and cons regarding screening, as outlined below. Urologists would always be happy to discuss these issues in more detail with patients before or during a screening process, such as in a patient with mildly elevated PSA or doubt about DRE findings. The Urological Society feels men should have the benefit of making their own decision about screening, rather than the 2 extremes of universal community screening, or total opposition by committees of people not aware of each individual's perception of the relative risks.

Summary

Prostate Cancer screening fulfils some, but not all of the criteria for an ideal screening program. The disease is common, causes the 2nd highest rate of male cancer deaths, and has a recognisable latent phase. However many men with prostate cancer die of other causes and the cancer deaths involve the older population with many competing morbidities. As a result, the "Person Years Life Lost" below 75 years are relatively few compared with other cancers and other causes of male deaths. Treatment benefits have not yet been proven in Randomised Controlled Trials, and treatments do carry some risks of morbidity. There is evidence that screening has discovered more cancers at a curable stage, but not yet evidence in a Controlled Trial that screening has reduced deaths from prostate cancer. Such trials are underway but it will be some years until results are available. In the meantime, men should have the option of screening for prostate cancer, providing they are given adequate information regarding the screening process before they make their decision.