

**Population-based
Screening for
Prostate Cancer
and Testing of
Asymptomatic Men in
New Zealand**

Final Report to the
National Health Committee



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KEY POINTS

The New Zealand Guidelines Group Prostate Cancer Screening Advisory Group offers the following conclusions to the National Health Committee about prostate cancer screening in New Zealand.

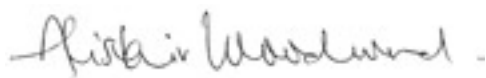
- Prostate cancer accounts for 3.8 percent of all male deaths in New Zealand; approximately two-thirds of these deaths occur amongst men aged 75 years and older. It is not known whether the incidence of prostate cancer for Māori men is more or less than for New Zealanders of European origin. The recent rise in the reported incidence of prostate cancer is largely due to widespread Prostate Specific Antigen (PSA) testing in general practice.
- Many men, their families and whānau, are concerned about prostate cancer and ask about prostate screening.
- Currently there is no evidence from RCTs that demonstrates whether or not population screening for prostate cancer has a positive effect on the mortality and morbidity from this disease.
- Advice on the benefits and harms of prostate cancer screening tests should be reviewed as new evidence emerges.
- Because of the lack of proven benefit and the potential for harm, screening for prostate cancer is not supported.

All members of the group agree that there is no evidence at this time to support an organised, publicly funded, screening programme. However, there was a spectrum of views within the advisory group on the issue of opportunistic screening. There are some who support offering the PSA test with full information on the risks and potential benefits of the test.

Others believe that because of the lack of evidence of benefit and potential for harm, men should not be offered PSA screening. If a man asks about PSA screening he should be given full information about the lack of evidence of benefit and potential for harm, and should be informed that PSA screening is not recommended in New Zealand.

All members of the group agreed that if a PSA test is being discussed, the decision to use a screening test should be made by an individual, with his family, whānau and his doctor with full information of the benefits and harms associated with PSA testing.

The NZGG Prostate Cancer Screening Advisory Group believes that a range of stakeholders should be invited to comment on the evidence in this report and the issues concerned with opportunistic screening.



Alistair Woodward
Chairman
NZGG Prostate Cancer Screening Advisory Group

SUMMARY

OF THE EVIDENCE ON POPULATION-BASED SCREENING FOR PROSTATE CANCER AND TESTING OF ASYMPTOMATIC MEN IN NEW ZEALAND

The following report represents the conclusions of the NZGG Prostate Cancer Screening Advisory Group. It is based on a systematic review of population screening for prostate cancer¹ and each heading is referenced to the relevant section of this review. In addition, references to the original source documents are provided for the supporting statements and other references are given for any statements that are not part of the systematic review.

- 1 Prostate cancer is an important cause of morbidity and mortality in New Zealand. It is the most commonly diagnosed cancer in men and the third most common cause of male cancer deaths. It is largely a disease of older men. Incidence, mortality rates, and trends are similar to those in other western countries. There is widespread opportunistic screening for prostate cancer in New Zealand general practice² and this is the most likely explanation for the recent rapid increase in the reported incidence of prostate cancer.**

(Population screening for prostate cancer. A systematic review. Pages 24-31)

- 1.1** Since 1991, there has been a rapid increase in the reported incidence of prostate cancer in New Zealand. The increase in the registration of new cancers reached a peak in 1995 and has fallen slightly since then. The most likely explanation for the increased incidence is the increased use of PSA testing in asymptomatic men.³
- 1.2** The majority (60%) of new registrations for prostate cancer are in men aged 70 years or older. In 1998, 65.3 percent of all deaths from prostate cancer were in men aged 75 years or older and 2.1 percent of prostate cancer deaths were in men aged less than 60 years. The registration rate for new prostate cancers in Māori is lower than for non-Māori (71.3 per 100,000 population compared with 96.2 per 100,000 population), but the rates in Māori men are based on relatively small numbers, and there has been variable recording of ethnicity data, so the estimates for Māori men are less robust.³
- 1.3** Nearly all general practitioners in New Zealand claim to be screening for prostate cancer in some men. For the majority of general practitioners this is by PSA testing with or without digital rectal examination (DRE). Men who ask their general practitioner about screening for prostate cancer are very likely to be offered a PSA test.⁴

- 1.4 The age-standardised mortality rate for prostate cancer in New Zealand in 1998 was 18.0 per 100,000 for the total male population. This rate had increased steadily until 1989 but between 1989 and 1998 there was a 5.3 percent decrease in the rate. These changes are consistent with similar trends of increased incidence and falling mortality rates in other developed countries.¹
- 1.5 There was an increase in the annual mortality rate for Māori of 77 percent between 1996 and 1998. In 1996 the Māori rate was lower than the non-Māori rate and in 1998 it was 55 percent higher. The age-standardised mortality rate in 1998 was 17.6 for the non-Māori population compared with 27.2 for the Māori population. It is likely that the changes in population data definitions and variable recording of ethnicity data have contributed to some of this disparity.⁵

2 Ecological studies of prostate cancer screening do not provide evidence that the decrease in prostate cancer mortality in New Zealand is likely to be due to prostate cancer screening.

(Population screening for prostate cancer. A systematic review. Pages 31-33)

- 2.1 The 5.3 percent decrease in prostate cancer mortality in New Zealand from 1989 to 1998 cannot be due to the increase in PSA screening,¹ as the timing is wrong. If screening for prostate cancer is effective in reducing mortality, it is likely that any reduction in the mortality rate due to screening will occur at least 7 years and possibly as much as 15 years after the start of screening. The true lead-time between diagnosis at screening and the presentation of symptomatic prostate cancer is uncertain and could be more or less than the suggested five to seven years.¹¹
- 2.2 Ecological studies in other countries have not provided consistent evidence that either supports or refutes an association between increased PSA screening and falling mortality rates.⁶⁻¹⁰

3 Estimates of the prevalence of prostate cancer greatly over-estimate the number of clinically significant prostate cancers. Screening for prostate cancer is likely to detect many prostate cancers that would never have caused any morbidity or mortality.

(Population screening for prostate cancer. A systematic review. Pages 36-37)

- 3.1 Post-mortem studies show that histological evidence of prostate cancer is very common and increases with age. Generally accepted figures for the prevalence rate of any form of prostate cancer are 15-24 percent for men aged 50 to 59 years, increasing to 39-44 percent for men aged 70 to 79 years, but these data may include some histological changes, which would not now be recognised as cancer.^{12, 13}
- 3.2 These figures greatly overstate the prevalence of localised prostate cancer that has the potential to progress to overt disease. The best estimates for the prevalence rate of clinically significant cancers is 4.4 percent in men aged 50 to 59 years, increasing to 11.4 percent in men aged 70 to 79 years.^{14, 15}

- 3.3 Current indications are that even the lowest estimates for the prevalence of disease detection at post-mortem are greater than the frequency of clinically significant localised prostate cancer, so that there is a potential for detecting many more tumours than will ever present clinically.¹
- 4 The disease specific survival rates for men with well – and moderately well – differentiated tumours, who are not given curative treatment, are approximately 90 percent at ten years. Between 70 percent and 83 percent of screen-detected, organ confined cancers are well – or moderately well – differentiated tumours.**
(Population screening for prostate cancer. A systematic review. Pages 12-14 and pages 41-42)
- 4.1 The best predictor of tumour progression and metastasis and, therefore, of survival rate is the histological grade of the tumour. Most studies reporting long-term survival rates for the different histological grades of prostate cancer use the Gleason scoring system. The degree of histological differentiation of the cancer cells is given a score between two and ten and these scores are usually grouped into well – differentiated (score 2-4), moderately – differentiated (score 5-7) and poorly – differentiated tumours (score 8-10). There are no long-term studies of survival which use more accurate methods of identifying the tumours that are most likely to progress.^{12,13,16-18}
- 4.2 The best estimates for disease specific survival suggest an 87-92 percent 10-year survival for well – differentiated and moderately – differentiated tumours. The 10-year survival rate for poorly – differentiated tumours is in the region of 44 percent. One study estimated the case fatality rate for untreated prostate cancer as 22 percent up to the age of 85 years.^{1, 12, 13}
- 4.3 Age has no significant prognostic effect on the rate of progression of prostate cancer and aggressive tumours are not more common in younger men compared with older men.¹⁹
- 4.4 None of the studies of survival rates are for screen-detected cancers. The cancers for the majority of men in these studies were detected because of clinical symptoms. Survival rates for prostate cancer detected at screening are likely to be better than these estimates because of the lead time between cancer detected by screening and prostate cancer presenting with clinical symptoms,¹ and the tendency for screen-detected tumours to be slower growing.
- 4.5 The results of the first screening round in 15,502 men, in the European Randomised Control Trial in Finland and the Netherlands, found that between 77 percent and 92 percent of cancers were organ confined and of these between 88 percent and 92 percent were well – or moderately – differentiated tumours.^{20, 21}

5 It is not possible to calculate exact values for the efficiency of screening tests for prostate cancer (DRE and PSA). The best estimates for the sensitivity and specificity of the PSA test are 74-84 percent and 90-94 percent respectively. Screening will give rise to a significant number of false-positive and false-negative results.

(Population screening for prostate cancer. A systematic review. Pages 48-51)

- 5.1 It is not possible to derive exact estimates of sensitivity and specificity for the DRE and PSA test because there is no available reference (gold) standard that can be applied to all individuals.
- 5.2 The positive predictive value of these tests varies with the prevalence of prostate cancer in the population and is, therefore, specific to each population studied.
- 5.3 The best estimates for the DRE are a sensitivity of 55-69 percent and a specificity of 89-97 percent. It is likely that the true values for this test are at the lower end of these ranges.^{12, 14, 15, 22}
- 5.4 Assuming that the true prevalence rate of clinically significant localised prostate cancer is 5.6 percent in men aged 55 to 69 years in New Zealand, then a sensitivity of 55 percent and a specificity of 89 percent would produce the following results for every 1000 men screened by DRE:
 - 135 men would have a positive DRE and would be referred for biopsy
 - 25 men with prostate cancer would be missed
 - 104 of the 135 men with a positive DRE would not have cancer and would have an unnecessary biopsy
 - 31 men with a positive DRE would have prostate cancer. In some of these men the cancer would not otherwise have become clinically evident in their lifetime.
- 5.5 The best estimates for the PSA are a sensitivity of 74-84 percent and a specificity of 90-94 percent. It is likely that the true values for this test are at the lower end of these ranges.^{12, 13, 23-26}
- 5.6 Assuming that the true prevalence rate of clinically significant localised prostate cancer in New Zealand is 5.6 percent in men aged 55 to 69 years, then a sensitivity of 74 percent and a specificity of 90 percent would produce the following results for every 1000 men screened (by PSA):
 - 136 men would have a PSA \geq 4.0 ng/ml and would be referred for biopsy
 - 15 men with cancer would have a PSA $<$ 4.0 ng/ml and would be missed
 - 95 of the 136 men with a PSA \geq 4.0 ng/ml would not have cancer and would have an unnecessary biopsy
 - 41 men with a PSA \geq 4.0 ng/ml would have prostate cancer. In some of these men the cancer would not otherwise have become clinically evident in their lifetime.

5.7 Screening that uses both DRE and PSA, and requires either a positive PSA test or a positive DRE as an indication for biopsy will result in a small increase in the detection rate of prostate cancer but a larger increase in the false-positive rate (more unnecessary biopsies). It is not possible to calculate accurate figures for using both tests together in this way, but for every 1000 men screened approximately one less cancer would be missed and 40 additional men would be wrongly identified as having cancer. Omitting the DRE and using only the PSA test but with a lower cut-point of ≥ 3.0 ng/ml (instead of 4.0 ng/ml) reduces the number of unnecessary biopsies but with only a small decrease in the detection rate.²⁷

6 Refinements of the PSA test do not add significantly to the efficiency of the test in a screening setting. Free-to-total PSA for PSA values between 4.0 ng/ml and 10.0 ng/ml will reduce the proportion of false-positive results but it is doubtful whether this will be sufficient to persuade many men not to have a prostate biopsy.

(Population screening for prostate cancer. A systematic review. Pages 51-52)

6.1 PSA density, PSA velocity and age-adjusted PSA cut-points do not make a useful contribution to improving the sensitivity and specificity of the PSA test. Age-adjusted cut-points increase sensitivity and reduce specificity in younger men and have the reverse effect of reducing sensitivity and increasing specificity in older men.²⁸

6.2 Free-to-total PSA measurements for PSA values between 4.0 and 10.0 ng/ml improves the sensitivity of the test and reduces the number of false negative results. A man with a PSA result between 4.0 and 10.0 ng/ml has an approximately 1-in-4 chance of having prostate cancer. If this same man then has the free-to-total PSA measured and the result is negative then this may reduce his chance of having prostate cancer to 1-in-12.²⁹

7 Screening for prostate cancer will detect clinically localised cancers at a stage when curative treatment may be possible. The likely detection rate for all cancers is between 2 percent and 4 percent of the screened population. It is not known what proportion of these cancers would have caused any morbidity or mortality.

(Population screening for prostate cancer. A systematic review. Pages 49-51)

7.1 In the initial screening round, in men aged 55 to 69 years, approximately 10 percent (range 7-15 percent) will have a PSA test of ≥ 4.0 ng/ml and one out of every four prostate biopsies at the first screening round will detect prostate cancer. This will give an approximate initial detection rate of between 2 percent and 4 percent.³⁰

7.2 There is no good evidence about the detection rate with repeated screening, but it is likely that this will fall to about 1 percent or less.³¹⁻³⁴

7.3 Screening using a PSA test ≥ 4.0 ng/ml, as the cut-point for an abnormal result will miss approximately 25 percent of prostate cancers.¹

7.4 The proportion of men that will be found by a screening programme to have prostate cancer, but who will not die from their prostate cancer, is not known. In the published results of the European RCT 91 percent-92 percent of cancers were well - differentiated or moderately well - differentiated tumours and earlier non-screening studies have found a 90 percent ten-year survival for men with these tumours.³⁰

8 Screening has the potential to cure some men of their prostate cancer before it causes any problem, but there is no good evidence of any improved mortality or benefit from screening for prostate cancer. The available treatments cause significant harm in a proportion of men. These harmful effects include impotence, urinary incontinence, diarrhoea, and death. It is likely that some men will suffer these consequences as a result of treatment for a prostate cancer that would have never caused any symptoms.

(Population screening for prostate cancer. A systematic review. Pages 60-61)

- 8.1 Screening for prostate cancer with the PSA test will identify many of the potentially curable and clinically significant cancers. The detection rate varies with different populations and screening protocols, but an average detection rate is of the order of 3 percent.³⁰
- 8.2 It is likely that curative treatment (eg, radical prostatectomy or radiotherapy) for men identified with localised prostate cancer will prevent progression of the disease and death from prostate cancer in some men.
- 8.3 Some men will suffer from the harmful effects of treatment for a condition that they would never have been aware of if they had not undergone the screening process.
- 8.4 There are potentially both psychological and physical harmful effects from the screening process. The psychological effects include increased anxiety levels in men with false-positive results and false reassurance for men with false-negative results.³⁷
- 8.5 The main physical harmful effects are pain, bleeding and infection in relation to the prostate biopsy. A very small proportion of men will have life-threatening infections as a result of their prostate biopsy. The reported complication rates vary widely. One screening study of 1,687 transrectal ultrasound-guided systematic sextant biopsies identified:
- haematuria or haemospermia in the three months following the biopsy in approximately one-third of men
 - pain after the procedure in 7.5 percent (126 men)
 - urinary retention in 0.4 percent (7 men)
 - fever >38.5°C in 4.2 percent (71 men). 6 men required hospital admission with one man requiring admission to the intensive care unit with sepsis and shock
 - two men developed allergic reactions to the antibiotic prophylaxis given routinely to all men before the biopsy.³⁸

- 8.6 The harmful effects of screening include the complications and side effects of treatment in men found to have prostate cancer. These are both the immediate mortality and morbidity of the treatment, and the possible long-term complications such as sexual dysfunction, urinary incontinence, and bowel dysfunction. An inevitable consequence of screening is that some men will experience the complications of treatment for a condition that would never have caused them any problem.
- 8.7 There is a wide variation in the reported complication rates^{39, 40}. Studies use different definitions of the complications and different methods of assessment, and many reports are from tertiary and specialist centres, which are unlikely to be representative of the experience of the majority of men in a population-screening programme. The best estimates of the complications rates are:
- a mortality rate within 1 month of surgery of less than 1 percent for men aged less than 75 years
 - after radical prostatectomy 20-70 percent of men have reduced sexual function and 15-50 percent have urinary problems
 - after radiation therapy 20-45 percent of men have reduced sexual function, 2-16 percent have urinary problems and 6-25 percent have bowel problems.
- 8.8 A recent RCT of quality of life after radical prostatectomy compared men following radical prostatectomy and watchful waiting⁴¹. Erectile dysfunction occurred in 80 percent of men after surgery compared with 45 percent of men in the watchful waiting group. After prostatectomy 56 percent of men were moderately or greatly distressed from compromised sexuality compared with 40 percent of men in the watchful waiting group. In the same study 49 percent of men had symptoms of urinary leakage compared with 21 percent of men who had not had surgery, and 18 percent of men reported a moderate or severe degree of urinary leakage compared with 2 percent of men in the watchful waiting group. In contrast, obstructive urinary problems were more common in the men who had not had surgery but these symptoms caused less distress. Twenty-seven percent of men were moderately or greatly distressed by urinary problems at least 12 months after prostatectomy compared with 18 percent of men in the watchful waiting group. Both the men in the radical prostatectomy group and the watchful waiting group reported similar outcomes on measures of quality of life, and psychological and physical well-being.

9 Currently there is no evidence from RCTs that demonstrates whether or not population screening for prostate cancer has a positive effect on the mortality and morbidity from this disease.

(Population screening for prostate cancer. A systematic review. Pages 60-61)

9.1 There is an ethical requirement that the potential benefits of screening should clearly outweigh any potential risks or harmful effects. Screening encourages otherwise healthy, asymptomatic individuals to undergo tests to identify a disease that they do not necessarily perceive that they are at risk from. This is different from a doctor trying the best available treatment, despite defects in medical knowledge, to help a patient with a disease. When a well person is offered a screening test there should be conclusive evidence that screening can alter the natural history of the disease in a significant proportion of those screened⁴².

In screening for prostate cancer some individuals will suffer significant harm and even death as a result of screening.

9.2 As the results of screening are not predictable, the results of well-organised RCTs must be assessed before deciding to offer screening⁴³. Reviewers of this topic conclude that there is insufficient evidence to determine whether screening for prostate cancer will have any positive effect.¹

9.3 There are ongoing RCTs and the results of these trials may provide evidence for the benefits of prostate cancer screening in the future.³⁰

9.4 The NZGG Prostate Cancer Screening Advisory Group has reviewed the recently released Screening to Improve Health in New Zealand, issued by the National Health Committee. A brief assessment of prostate cancer testing has been undertaken using this framework, and will be forwarded separately to the NHC. PSA screening for prostate cancer does not satisfy the criteria, as it does not have proven benefit, and has the potential for harm.

10 Prostate cancer accounts for 3.8 percent of all male deaths.³ The recent rise in the reported incidence of prostate cancer is largely due to widespread PSA screening in general practice. There is no evidence that the 5.3 percent decrease in prostate cancer mortality is due to screening. Many men and their families and whānau are concerned about prostate cancer and ask about prostate screening. The decision to be screened should be made with full information by the man, his family, whānau and his doctor. Men considering a PSA test should be given detailed information about the limitations of the screening tests and the possible diagnostic and treatment choices they may face. They should also be informed that on the basis of the current evidence it is not known if screening will reduce their chances of dying from cancer.

(Population screening for prostate cancer. A systematic review. Pages 15, 24-28)

10.1 Since 1991 there has been a rapid increase in the reported incidence of prostate cancer in New Zealand. In 1998 there were 524 deaths from prostate cancer and 2494 new cases. This is 13 percent of all male cancer deaths and 27 percent of all new male cancers registered in 1998. Although evidence does not yet support screening for prostate cancer, there is growing public concern and a considerable demand for the PSA test by men worried about the disease. The recent rapid increase in prostate cancer incidence is largely due to widespread PSA testing in New Zealand general practice.

10.2 Localised prostate cancer does not usually produce symptoms. The lower urinary tract symptoms (LUTS) of frequency, urgency, hesitancy, and terminal dribbling are usually the result of benign prostatic hyperplasia (BPH). LUTS are also the most common presenting symptoms of prostate cancer and result from involvement of the urinary tract and bladder neck by the enlarged prostate gland. This is usually at a stage when curative treatment is no longer possible. There is no evidence to suggest that men with LUTS or BPH have an increased risk of prostate cancer⁴⁴. The absence of any good evidence supporting an association between LUTS or BPH and prostate cancer means that the decision, whether or not to test for prostate cancer, should be the same as the decision, whether or not to screen an asymptomatic man, with the same requirement to fully counsel the man on the implications of the test.

10.3 An increasing number of men and their whānau are sufficiently anxious about prostate cancer to seek help, principally by asking for a PSA test. At the moment some men are being offered a PSA test but in an unstructured and sometimes ill-informed way, whilst others are currently dissuaded from having a PSA test because of the policy on population screening⁴. Any man considering a PSA test should be given detailed information about the performance of the test, and the possible further diagnostic and treatment choices with which he may be faced. They should also be informed that on the basis of current evidence it is not known if screening will reduce their chances of dying from prostate cancer and that screening is not currently recommended by the National Health Committee.

10.4 A recent study published in the Journal of Medical Screening⁴⁵ shows that Australian men who received an evidence-based booklet designed to promote informed decision-making for men considering PSA screening had significantly improved decision-making and lower levels of decisional conflict, even amongst passive decision makers. The advisory group has reviewed examples of evidence-based advice published in Australia and the United Kingdom for health care practitioners, and information for men, their families and whānau. It is suggested that this material could be used to assist in drafting further information for New Zealand men.

11 Assessment of the current screening, diagnosis and management of prostate cancer in New Zealand is seriously handicapped by the lack of information about the frequency of PSA testing, the frequency of the different treatments for prostate cancer and the outcomes of these treatments.

11.1 The importance of prostate cancer and the existing and potential costs to the New Zealand health care system suggest that collection of this information should be made a priority. For the same reason, any educational material about screening for prostate cancer that is made available to health care practitioners, men, their families and whānau should be fully evaluated for its effectiveness.

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COMPOSITION OF THE ADVISORY GROUP

MEMBERS OF THE NZGG PROSTATE CANCER SCREENING ADVISORY GROUP

Alistair Woodward (Chair)	National Health Committee, Professor of Public Health, Wellington School of Medicine and Health Sciences, University of Otago
John Childs	Consultant, Radiation Oncology, Auckland
Peter Davidson	Consultant Urological Surgeon, Christchurch
Betsy Marshall	Policy Advisor, Cancer Screening & Cancer Control, Cancer Society of New Zealand, Auckland
Jim Vause	General Practitioner, Blenheim Representative from the Royal NZ College of General Practice
John McMenamin	General Practitioner, Representative from the Royal NZ College of General Practice
Barry Young	Chair, Prostate Awareness and Support Society, Auckland
Terry Ehau	Ngati Porou Hauora, East Coast
Ann Richardson	Epidemiologist, Christchurch School of Medicine, University of Otago
Brett Delahunt	Professor of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago

EX OFFICIO

Ashley Bloomfield	Public Health Leader - Population Health Screening, National Screening Unit, Ministry of Health
John Durham	General Practitioner / Researcher
Emma Sutich	NZGG Project Manager (until December 2002)
Catherine Marshall	CEO, NZGG
Stephanie Dixon	Office Manager, NZGG



NATIONAL ADVISORY COMMITTEE
ON HEALTH AND DISABILITY
HUNGA KAITITIRO I TE HAUORA O TE TANGATA

**Incorporating the Public Health Advisory Committee
Te Rōpū Tohutohu i te Hauora Tūmatanui**