



Inquiry into early detection and treatment of prostate cancer

Report of the Health Committee

Forty-ninth Parliament
(Dr Paul Hutchison, Chairperson)
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1 Introduction

We initiated this inquiry in an attempt to recommend to the Government clear messages to be given to men relating to the early detection and treatment of prostate cancer. In the past conflicting messages have been sent, leading to confusion on this matter.

We are grateful to and respectful of the submitters, men's groups, clinicians, and epidemiologists who contributed to this inquiry, all of whom are motivated by a wish to improve men's health. We have faced difficulty caused by the different interpretations of the changing literature evidence base. Given the changing state of knowledge, men should be encouraged to seek up-to-date evidence-based information from their general practitioners about the advantages and disadvantages of screening and treatment of prostate cancer so that they can make active, informed choices. This process should be part of a men's health assessment carried out at age 45, or earlier if they have known cardiovascular risk factors.

Our report also covers some of the controversies about the early detection and treatment of prostate cancer. We strongly recommend that, within a year of this report's presentation, the Ministry of Health work with all interested parties to establish a quality improvement programme relating to the early detection and treatment of prostate cancer.

Summary of recommendations

Following its inquiry, the Health Committee makes the following recommendations to the Government:

- that the Ministry of Health encourage and promote the case for men to seek up-to-date evidence-based information from their general practitioners about the advantages and disadvantages of screening and treatment for prostate cancer (p. 9)
- that the Ministry of Health encourage and promote the case for general practitioners' providing men with initial consultations about the advantages and disadvantages of screening and treatment for prostate cancer. The initial consultation should take place during the cardiovascular risk assessment which is recommended in the national guidelines, for men at the age of 45, or 10 years earlier for men with known risk factors (p. 9)
- that the Ministry of Health encourage general practitioners to advise men with a strong family history of prostate cancer that they have the choice of having their full history noted and then undergoing a clinical examination, PSA testing, and rectal examination from the age of 40 (p. 9)
- that it establish a quality improvement programme relating to the early detection and treatment of prostate cancer. The programme should ensure that all men with prostate cancer have fair access to good quality care (to be achieved within one year) (p. 26)

- that it fund the Ministry of Health to work with non-governmental organisations, groups of patients, and health professionals to set priorities and develop processes to implement a national quality improvement plan for the early detection and treatment of prostate cancer (to be achieved within one year) (p. 26)
 - that it continue research into the types of care received by men with diagnosed prostate cancer in New Zealand. The research should include equity issues, costs, and complications arising from types of care, and the proportion of men who undergo biopsy after a PSA test (p. 26)
 - that it ensure that general practitioners have available best-practice, evidence-based tools to help their patients understand the tests available for early detection and treatment of prostate cancer (p. 28)
 - that it ensure as many men as possible have access to reliable information on the early detection and treatment of prostate cancer (p. 28)
 - that the Ministry of Health develop a prostate cancer screening decision-aid, in close consultation with interested parties including the Royal New Zealand College of General Practitioners, the Urological Society of Australia and New Zealand, the Prostate Cancer Foundation of New Zealand, Cancer Control New Zealand, the New Zealand Guidelines Group, the New Zealand Society of Pathologists, and the New Zealand Cancer Society. We consider this should be available within 12 months of this report being presented (p. 29)
 - that the Ministry of Health continue to monitor international trials relating to the benefits and harms of prostate cancer screening. When new evidence arises, the Ministry of Health should update its policies on screening and prostate cancer (p. 37)
 - that the Ministry of Health endeavour to decrease any harms caused by unorganised prostate cancer screening (p. 37)
 - that the Ministry of Health continue to assess the advantages and disadvantages of prostate screening on the basis of the latest research and literature (p. 31)
 - that it support continued research into the early diagnosis and treatment of prostate cancer (p. 37)
 - that it undertake an analysis of the costs of the current unorganised prostate cancer screening in New Zealand (p. 37)
 - that it undertake a costing of a quality improvement programme for prostate cancer diagnosis and treatment, which should include the development of consumer information for men and their families; the analysis of current service delivery; the development and implementation of guidelines; and the development and implementation of national monitoring indicators (p. 37)
 - that it require the Ministry of Health to facilitate research into the side effects of investigative procedures such as Transrectal Ultrasound Guided biopsies, and into definitive treatment in the New Zealand context (p. 39)
 - that it require the Ministry of Health to establish national monitoring of prostate cancer management and analyse the data that it collects on an ongoing basis (p. 39).
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Background

Prostate cancer is the most commonly diagnosed cancer in New Zealand men and the third most common cause of male cancer deaths. Approximately 3,000 new cases of prostate cancer are diagnosed each year, and around 560 men die of the disease each year. We were advised that this mortality rate equals that of breast cancer.

There has been vigorous debate involving public groups, some clinicians, and epidemiologists about the value of screening for prostate cancer using the Prostate Specific Antigen (PSA) blood test, and the benefits of early detection and treatment. This has led to confusion amongst men as to what sort of action they should take.

In 2009, reports were released on two randomised trials of prostate cancer screening. The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, or PLCO, was completed in the United States of America,¹ and the European Randomised Study of Screening for Prostate Cancer, or ERSPC, in Europe.² It was hoped that these trials would clarify finally the benefit or otherwise of implementing an organised national screening programme for prostate cancer, or using the PSA test to screen men as part of an unorganised screening programme.

These trials did not establish that screening populations for prostate cancer has clear overall benefit. One of the trials found a 20 percent relative reduction of risk of death from prostate cancer in men who underwent screening compared with the control group, and the other found none. It was not established whether the benefits of screening outweighed the harm. Before organised screening can be advocated in New Zealand, further trial results will need to demonstrate that the benefits of screening outweigh the harms. The Göteborg study found that in order to prevent one death from prostate cancer, 293 men need to be screened and 12 men need to receive treatment.³ The Göteborg study showed a 44 percent reduction in mortality.

The 2004 Ministry of Health pamphlet *Screening for Prostate Cancer—Information for Health Care Practitioners* states that “there is good evidence that PSA screening can detect early-stage prostate cancer, but mixed and inconclusive evidence that early detection improves health outcomes.” Some submitters interpreted this message as the Ministry of Health discouraging men from undergoing screening. The National Health Committee’s statement in its 2004 report to the Minister of Health was explicit. It stated “The NHC does not recommend screening men without symptoms for prostate cancer, regardless of age, because the risks associated with screening and subsequent treatment exceed any benefits”.⁴ The Ministry of Health pamphlet was replaced by a show-card issued in 2005 and updated in 2007, which advised health practitioners to explain the potential benefits and harms of screening for prostate cancer and associated treatment. The 2008 New

¹ Andriole, GL, Crawford, ED, et al. “Mortality results from a randomized prostate-cancer screening trial”, *New England Journal of Medicine*, Vol. 360, 2009, pp.1310–1319.

² Schroder, FH, Hugosson, J, Roobol, MJ, et al. “Screening and prostate-cancer mortality in a randomized European study”, *New England Journal of Medicine*, Vol. 360, 2009, pp.1320–1328.

³ The Göteborg study is a randomised population-based prostate cancer screening trial conducted in Sweden.

⁴ National Health Committee, *Prostate Cancer Screening in New Zealand*, Wellington, p. 2.

Zealand Guidelines Group pamphlet *Testing for Prostate Cancer—Information for men and their families* does not discourage screening, but says:

A national screening programme for prostate cancer has not been established because results from good-quality research studies are required to confirm whether the benefits of screening outweigh the harms. Although a national screening programme for prostate cancer is not appropriate given current information, every man has the right to decide for himself whether or not to be tested to check for prostate cancer.

We agree with this emphasis and believe the Ministry of Health should encourage and promote the case for men to seek up-to-date evidence-based information from their general practitioner on the pros and cons of early testing and treatment of prostate cancer, so that they can make an active choice themselves.

We heard evidence from representatives of Cancer Control New Zealand, the Cancer Society of New Zealand, the New Zealand Guidelines Group, the Prostate Cancer Foundation of New Zealand, the Royal New Zealand College of General Practitioners, and urologist Dr Robin Smart, a member of the Urological Society of Australia and New Zealand. We worked with these submitters to draft the following statement:

The Health Committee understands that current national guidelines recommend that all men should visit their general practitioner for a formal cardiovascular risk assessment “warrant of fitness” at least at the age of 45, or 10 years earlier if they have known cardiovascular risk factors. This provides a valuable opportunity to review other general health issues with male patients. From the evidence of our inquiry we consider that at the same time men should be encouraged to have the choice of receiving consistent, clear, and accessible information on the pros and cons of prostate cancer testing. This evidence should be up-to-date and easily readable, and have reference to a website that contains more detailed material. (A standard video as used in some places around the world would achieve consistency.)

Men with a strong family history of prostate cancer should be advised of the choice of undergoing a full history, clinical examination, PSA testing, and rectal examination from the age of 40. This advice should include the limitations of current testing techniques. Men without a strong family history of prostate cancer should be given the choice, after discussion of the pros and cons, of undertaking clinical testing for prostate cancer (which includes PSA testing and/or rectal examination) from the age at which men have their cardiovascular warrant of fitness.

The Health Committee concludes that

there is evidence that shows PSA testing saves some lives but

this must be balanced against the known side effects of further investigation and treatment.

The Health Committee also concludes that

active surveillance rather than definitive treatment should be considered for some men.

Information to men, their partners, and GPs should be changed to reflect this evidence.

New Zealand men should be encouraged to make an informed choice.

The Health Committee does not advocate a national prostate screening programme at this stage, and it is aware of the need for a better (and more cancer-specific and sensitive) test than the current PSA test.

Men are encouraged to seek advice from their general practitioners, guided by the consensus statement above.

(We also note that the Australian Senate Select Committee on Men's Health concluded in its 2010 report that population-based screening is not justified. However, that committee supported testing where a man has general symptoms, has a family history of the disease, or wishes to monitor his own health status. The committee also endorsed the efforts of various non-governmental groups to make men more aware of the issues, and to encourage them to go to a doctor.)

Recommendations

1 We recommend to the Government that the Ministry of Health encourage and promote the case for general practitioners' providing men with initial consultations about the advantages and disadvantages of screening and treatment for prostate cancer. The initial consultation should take place during the cardiovascular risk assessment which is recommended in the national guidelines, for men at the age of 45, or 10 years earlier for men with known risk factors.

2 We recommend to the Government that the Ministry of Health encourage and promote the case for men to seek up-to-date evidence-based information from their general practitioners about the advantages and disadvantages of screening and treatment for prostate cancer.

3 We recommend to the Government that the Ministry of Health encourage general practitioners to advise men with a strong family history of prostate cancer that they have the choice of having their full history noted and then undergoing a clinical examination, PSA testing, and rectal examination from the age of 40.

Terms of reference

We established the following terms of reference for our inquiry:

1 To seek a summary of the contemporary literature on the subject, including incidence, mortality, groups at risk, testing options (with particular reference to age and family history, treatment and what other countries are doing). This will also include the results of the New Zealand Guidelines Group screening review, due in November 2009.

2 To seek opinions from

- affected and asymptomatic men, their families, patient advocacy groups including the Prostate Cancer Foundation and the National Screening Advisory Committee

- specialist clinicians, radiation oncologists, urologists, and general practitioners
 - epidemiologists, and those involved with the Ministry of Health, New Zealand Guidelines Group.
- 3 To seek best methods to promote awareness for early detection and treatment of prostate cancer.
- 4 To seek a cost-benefit analysis, if appropriate.

Conduct of the inquiry

We sought submissions from the individuals and groups specified in the terms of reference, and made a call for public submissions. We heard evidence between 14 October 2009 and 23 March 2011. We received both oral and written submissions from a variety of submitters, including the Prostate Cancer Foundation of New Zealand, the Royal New Zealand Returned and Services Association, the National Screening Advisory Committee, and the Urological Society of Australia and New Zealand.

We also received evidence from submitters on topics that fell outside the terms of reference for this inquiry.

Structure of the report

This report begins by explaining the nature of prostate cancer, the history of earlier inquiries, and current testing and treatment in New Zealand. It then details issues that submitters have reported as problematic, such as informed consent, inconsistency of approach in the medical community, a reported unwillingness by some doctors to test for prostate cancer, and the availability and quality of information. The next section addresses the controversial aspect of screening for prostate cancer, and the final section deals with prostate cancer treatment.

Advisers

To assist with the inquiry, the Minister of Health made two Ministry of Health officials, Dr John Childs and Dr Nina Scott, available as advisers. Dr Childs is the National Clinical Director of the Cancer Programme and an oncologist, and Dr Scott was the Māori Strategic Adviser for the National Screening Unit and is a public health physician. We also engaged Associate Professor Robert Scragg to assist with epidemiological advice. Professor Scragg is a specialist epidemiologist, and an independent and credible medical professional who we considered would not have preconceived views on the issue.

Acknowledgement

We sincerely appreciate the time and effort required of submitters who presented oral or written evidence to us. We understand the personal nature of many submitters' evidence and the courage needed to speak about these matters in public.

While we accept that this report can only recommend changes to the Government, we also hope it can clarify and improve the quality of the information given to the public on this issue.

Terminology used in this report

To assist readers, we have included a list of terminology used in this report.

Asymptomatic	Having no disease symptoms. Early/localised prostate cancer will not usually produce any symptoms.
Symptomatic	Having symptoms of the disease. Benign prostate hyperplasia usually produces symptoms.
Benign Prostate Hyperplasia	A benign (non-cancerous) enlargement of the prostate gland which commonly occurs in men as they age.
Brachytherapy	Radiation treatment for prostate cancer, which involves implanting permanent or temporary radiation sources (usually in the form of seeds or wire) in the prostate gland.
Coverage	The proportion of the potential target population that participates in a screening programme.
Digital rectal examination (DRE)	An examination in which a clinician inserts a lubricated, gloved finger into the rectum to feel (palpate) for abnormalities of the prostate and rectum.
Ecological study	A study that aims to detect associations between risk and exposure to risk factors and then suggest, or preferably confirm, explanatory hypotheses (ideas). The group rather than the individual constitutes the basic statistical unit.
False negative	A negative result from a screening test in a person who actually has the condition for which the test was performed.
False positive	A positive result from a screening test in a person who does not have the condition for which the test was performed.
Gleason score	A system of grading prostate cancer tissue based on how it looks under a microscope. Gleason scores range from 2 to 10 and indicate how likely it is that a tumour will spread. A low Gleason score means the cancer tissue is similar to normal prostate tissue, and the tumour is less likely to spread; a high Gleason score means the

	cancer tissue is very different from normal and the tumour is more likely to spread.
Incidence	The number of new cases arising in a given period in a specified population. This is usually reported as an age-specific rate, giving the number of new cases per 100,000 of the population in each age group for each year. It can be adjusted to an age-standardised rate, which allows for differences in the age distribution of populations being compared.
Metastasis	A secondary tumour that has spread from a primary source.
Opportunity cost	The opportunity forgone for one option as a result of allocating the resources in question to another option.
Opportunistic screening	Asking a person who is presenting to the health system for another reason a question or offering a test to detect the presence or confirm the absence of a specific condition. They may also self-present. Opportunistic screening is a recruitment method for both organised and unorganised screening.
Organised screening	Screening programmes characterised by quality assurance processes to ensure that the screening pathway is monitored and problems prevented, found and fixed. Organised screening programmes have varying levels of quality assurance. Opportunistic recruitment is a method of recruitment to both of New Zealand's current cancer screening programmes.
Over-diagnosis	Diagnosis of prostate cancer in men that would never have caused them problems in their lifetime.
Over-treatment	Any treatment for prostate cancer in over-diagnosed men.
Population screening programmes	Screening entire populations or a large and easily identifiable group within a population. The target population group for screening may be defined geographically or by some other characteristic such as gender, age, or ethnicity. The New Zealand cervical and breast screening

	programmes are examples of population screening programmes.
Prevalence	The number of cases in a defined population at a specified point in time.
Quality assessment	Measurement of performance and outcomes against standards.
Quality assurance	Detection and correction of problems, followed by ongoing monitoring of quality.
Quality improvement	Prevention of problems, control of unintended variations in process, and constant improvement through quality assessment and quality assurance.
Relative risk	The chance (probability) that an individual will develop a condition compared with the chance (probability) of that condition in the general population. In the case of PSA screening, the relative risk of dying from prostate cancer is the chance (probability) of someone in the PSA-screened group dying from cancer, compared with the chance (probability) of someone in the non-PSA-screened group doing so.
Relative risk reduction	The difference in the probability that a condition occurs in one group exposed to an intervention compared with another group which is not exposed to an intervention, expressed as a proportion of the probability in the unexposed group. For PSA screening this is the difference in the chance of dying from prostate cancer in the screened group compared with the non-screened group, divided by the chance of dying in the non-screened group.
Screening	A health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to determine whether they are more likely to be helped than harmed by further tests or treatments to reduce the risk of disease or its complications.
Screening pathway	The screening process from a participant's perspective. It includes the following steps:

	<ul style="list-style-type: none"> • an invitation to be screened in an organised or unorganised screening programme, via a letter of invitation or via opportunistic invitation • provision of information about the purpose of the screening, the possibility and likelihood of false positive or negative results, the uncertainties and risks of the screening process, and its medical, social or financial implications • undergoing the screening test • receiving the screening test results • other investigations and diagnostic procedures to confirm or exclude a cause for the positive screening test • treatment if decided on • monitoring and evaluation and quality improvement at all these stages.
Sensitivity	The proportion of people in the screened population who have the condition in question and are correctly identified (by the screening test) as having the disease.
Specificity	The proportion of people in the screened population who do not have the condition and are correctly identified (by the screening test) as not having the condition.
Surveillance	The monitoring of people known to have a disease or to be at increased risk of a disease.
Under-diagnosis	Not being diagnosed with a condition that causes problems later in one's lifetime.
Under-treatment	Lack of treatment because of under-diagnosis.
Unorganised screening	Ad hoc screening programmes, characterised by a lack of quality processes such as monitoring and evaluation. Because of the lack of attendant quality processes their safety, effectiveness, and cost-effectiveness cannot be assessed and guaranteed.

2 What is prostate cancer?

Prostate cancer is a major health issue for men worldwide. Found only in men, the prostate gland surrounds the urethra where it leaves the bladder, and produces a fluid that is a component of semen. Acute and chronic prostatitis and prostatic enlargement are other medical problems that can affect the prostate gland. With ageing of the population, it is predicted that prostate cancer will become the leading cause of male cancer deaths in the near future.

It has previously been accepted that prostate cancer affects only older men, and that most men will die with the disease, not because of it. This view is no longer accepted by many health professionals, who have had to treat men as young as 40 years of age with aggressive forms of the disease.

Risk factors for prostate cancer

We understand that a major case control study carried out in New Zealand found only one risk factor for prostate cancer other than age, which is a history of prostate cancer in first-degree relatives. The lack of modifiable risk factors for prostate cancer means that primary prevention strategies are not possible, which means reliance on other strategies for reducing mortality, such as screening and improving treatment.

Age

Age is the strongest risk factor for prostate cancer. The incidence of the disease rises with age; older men are more likely to be diagnosed with, and to die of, prostate cancer. There is no significant evidence, however, that older men are more likely to develop more aggressive prostate cancer.

Family history

We understand that approximately 5 to 10 percent of prostate cancer cases are thought to have a substantial inherited component. The relative risk of prostate cancer doubles with one first-degree relative diagnosed at age 70 or under, and is four times more likely with two diagnosed relatives, if one was diagnosed before turning the age of 65. The risk of contracting the disease increases by seven to 10 times with three or more affected relatives. In some men with a family history gene mutations which may be inherited have been found.

Environmental factors

A diet high in animal fats and protein may increase the risk of developing prostate cancer. It is unknown what environmental factors are protective for prostate cancer.

Figure 1 Age-specific rates per 100,000 for the five most common causes of cancer death, 2008 (Ministry of Health, 2011)

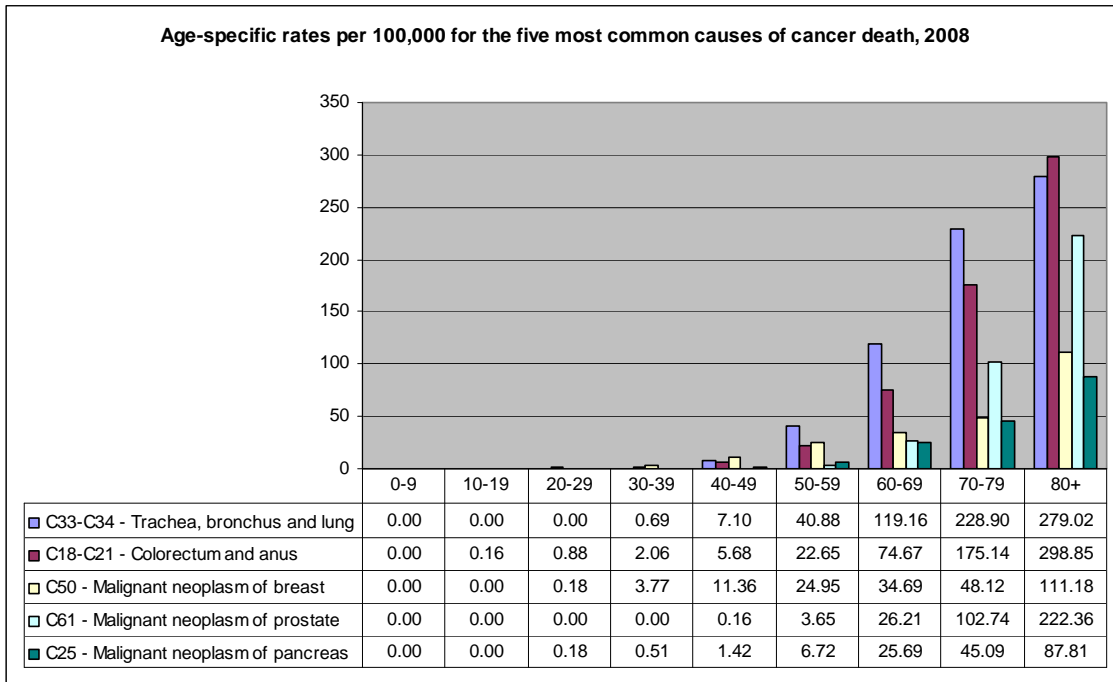
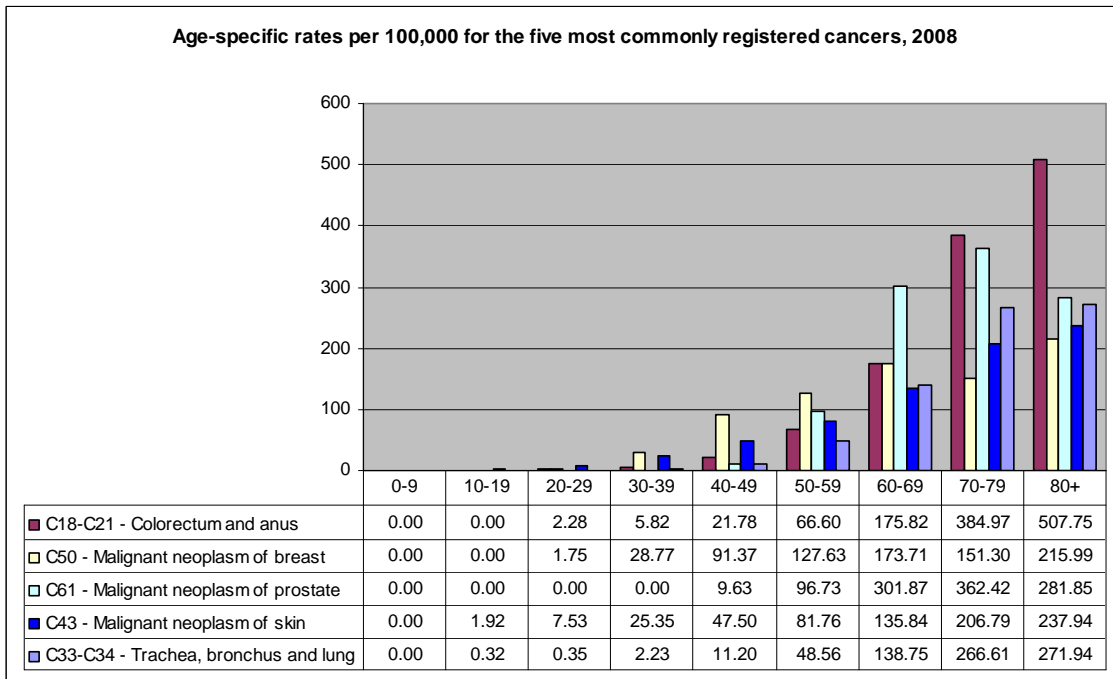


Figure 2 Age-specific rates per 100,000 for the five most commonly registered cancers, 2008 (Ministry of Health, 2011)



Ethnicity

Although ethnic groups have different incidences of prostate cancer, the reasons for this are unclear. The incidence of prostate cancer in African Americans is twice that among white Americans. In New Zealand non-Māori men are more likely to be diagnosed with prostate cancer than Māori men.

Table 1 Summary of prostate cancer registrations and deaths, 2008 (Ministry of Health, 2011)

	Total	Māori
New cases registered per year	2939	141
Incidence	103.3 per 100,000 men in New Zealand	81.9 per 100,000 Māori men
Mortality/deaths per year	670	35
Mortality rate	21.5 per 100,000 men in New Zealand	25.6 per 100,000 Māori men
Relative risk of dying from prostate cancer after diagnosis for Māori compared with non-Māori. Adjusted for differences in age and stage (including extent of cancer spread) at time of diagnosis.		2.04

Incidence and mortality for Pacific Island men

Pacific incidence and mortality rates cannot usefully be analysed separately because numbers are too small to convert into meaningful rates. However, Pacific data is reported from the cancer registry.

Table 2 Number of deaths from prostate cancer by ethnicity (Cancer Registrations, 2008) (Ministry of Health, 2011)

	Māori	Pacific	Non-Māori, Non-Pacific	Total
Malignant neoplasm of prostate	35	15	620	670

Reducing the risk

Although prevention was not in the terms of reference for this inquiry, we received a submission on the question of whether low selenium is a risk factor for prostate cancer. The submission cited the Selenium and Vitamin E Cancer Prevention Trial, which began in 2001.⁵ This study has recently been stopped, because no differences appeared in the risk of prostate cancer between men receiving selenium and vitamin E and the control group.

⁵ The Selenium and Vitamin E Cancer Prevention Trial was a clinical trial to see if one or both of these substances prevent prostate cancer when taken as dietary supplements.

Other studies are being conducted on how to reduce the risk of developing prostate cancer in men with high PSA levels but no detectable cancer. The reduction of risk would reduce the need for men to undergo repeated biopsies to monitor their condition. Various approaches are being studied, including vitamins, micronutrients, 5-alpha-reductase inhibitors, non-steroidal anti-inflammatory drugs, and selective oestrogen receptor modulators. To our knowledge, we are unaware that any of these approaches have been shown to be effective.

Medical controversy surrounding prostate cancer

There is some controversy over the efficacy of the PSA test as a screening test for prostate cancer. There is more controversy about whether a population-based, organised prostate cancer screening programme, such as that implemented for breast cancer, should be started. There are also concerns about outcomes, and about morbidity or side effects from treatment. Submitters told us that the medical controversy means that some doctors either do not inform them about prostate cancer, or do not encourage them to be tested. Many individual submitters told us that they struggled to obtain informed or balanced information from their doctors.

We were informed that unlike many other cancers, changes to the prostate gland are not immediately obvious and symptoms are slow to appear. By the time symptoms do appear the cancer may have metastasised and can be much harder to treat and more likely to be fatal. The only definitive test for the disease is a biopsy, an invasive procedure that involves taking tissue samples from the prostate for examination. However, if a biopsy is not performed until symptoms have appeared, there is an increased risk of death from the disease.

We were advised that older reports based on a Detroit study had estimated that 32 percent of men in the fifth decade of life had occult cancer.⁶ More recent reports using newer methods of histochemical analysis have shown that many tumours with low Gleason score that were previously classified as prostate cancer are benign lesions and more recent studies estimate that the true incidence of occult cancer in men under 50 years is about 5 percent.⁷

We were advised that although most men's prostate cancer grows at a slow rate, there is a progressive increase in deaths from the disease 15 to 20 years after diagnosis. Data such as this has led to recommendations that men's treatment be managed by active surveillance or watchful waiting, particularly for men whose clinical assessment has concluded that they have low-risk cancers. This data has also led to the practice of offering screening to younger men because a young man's prostate cancer is more likely to progress over his lifetime if left untreated.

⁶ Sakr, W A, Haas, G P, et al., "The frequency of carcinoma and intraepithelial neoplasia in young male patients", *J Urol*, 150, 1993, pp. 379–385.

⁷ Ries, L A G, Miller, B A, et al. (editors), *SEER Cancer Statistics 1973–91: Tables and Graphs*, Bethesda, National Cancer Institute, 1994 and Smart, R F, "Screening for prostate cancer: a review of the evidence in 2009", *CML-urology* 15(3), 2009, pp. 61–73.

Prostate specific antigen test

We were advised by the Ministry of Health that the prevailing view of public health epidemiologists is that the PSA test is not definitive because it cannot determine with enough accuracy whether a) the man tested does or does not have prostate cancer, or b) if he does have prostate cancer, whether the cancer is indolent or passive and unlikely to have significant ill effects or cause death, or is aggressive and has metastasised beyond the prostate itself, so likely to lead to serious illness and death.

They consider that the PSA test does not have a high degree of either sensitivity (the ability to indicate a reliable positive result) or specificity (the ability to reliably indicate the absence of the disease). We were advised that in the view of public health epidemiologists, the weakness of the test means some men are being subjected to under-treatment (because some cancers are missed, and those men die), and some to over-treatment (because they are subjected to sometimes severe side-effects from treatment for cancers that are passive).

Recent studies have produced conflicting results and interpretations, and failed to settle the debate. They highlighted continued uncertainty about the use of the PSA test in screening programmes for prostate cancer.

We are aware that a 2009 report of the Australian Senate Select Committee on Men's Health concluded that organised population-based screening is not justified at this stage. However, the committee supported testing where a man has general symptoms, has a family history of the disease, or wishes to monitor his own health status. That committee also endorsed the efforts of various non-governmental groups to make men more aware of the issues and to encourage them to go to their doctors.

Comparison of PSA sensitivity and specificity with other cancer screening tests

Studies report a range of estimates of the sensitivity and specificity of PSA testing. Estimates based on systematic reviews suggest that PSA sensitivity ranges from 43 to 73 percent and specificity from 56 to 97 percent. Table 3 compares these factors with mammography, cervical pap smear, and faecal occult blood screening tests.

The reasons for variation for PSA testing sensitivity and specificity include the cut-off levels used (the level at which the test is assessed to be positive and warrant further investigation) and verification bias, where not all men in the study have a confirmatory biopsy. Other factors which influence PSA sensitivity include prior PSA testing of populations and differing thresholds for TRUS biopsy. When a lower PSA test cut-off level is used the sensitivity increases but the specificity is reduced. The implication is that there is no safe cut-off PSA level and men may have a risk for prostate cancer despite a negative test, and conversely that a positive test does not mean that prostate cancer is present.

Table 3: Comparison of sensitivity and specificity for cancer screening tests

Screening test	PSA test	Mammography	Cervical smear	Faecal occult blood
Cancer screened	Prostate cancer ⁸	Breast cancer ⁹	Cervical DCIS ¹⁰	Bowel cancer ¹¹
Sensitivity	43–73%	63–97%	40%–81%	5.4%–83%
Specificity	56–97%	91–97%	75%–98%	65%–99%

Estimates of PSA sensitivity and specificity from the ERSPC suggest that the positive predictive value (PPV) for the PSA test which is a function of sensitivity, specificity, and disease prevalence, may be better than that for mammography. PPV from the ERSPC and Göteborg were reported as 21 percent and 24 percent respectively, which compares with a range of 3 percent to 21 percent reported for breast cancer screening. Clinical practice which does not require an automatic biopsy for all men with a PSA above a level of 4.0 ng/ml may lead to a higher PPV.

⁸ New Zealand Guidelines Group, *Update of Evidence for Prostate-Specific Antigen (PSA) Testing in Asymptomatic Men*, 2009.

⁹ <http://breastscreening.cancer.gov/data/benchmarks/screening/2009/tableSensSpec.html>, last accessed 7 July 2011.

¹⁰ Nanda, K, McCrory, D C, et al., “Accuracy of the Papanicolaou test in screening for an follow-up of cervical cytologic abnormalities: a systematic review”, *Ann Intern Med*, 132 (10), 2000, pp. 810–19; Rogoza, Raina, et al. “Optimization of primary and secondary cervical cancer prevention strategies in an era of cervical cancer vaccination: a multi-regional health economic analysis”, *Health Economics of HPV Vaccination for Cervical Cancer Prevention: Historical Developments and Practical Applications*, Volume 26, Supplement 5, 15 September 2008, pp. F46–F58.

¹¹ Burch, J A, Soares-Weiser, K, et al., “Diagnostic accuracy of faecal occult blood tests used in screening for colorectal cancer: a systematic review”, *J Med Screen*, 14 (3), 2007, pp. 132–7.

3 Prostate cancer in New Zealand

Earlier inquiries

National Health Committee report 2003

In 2001 the National Health Committee (NHC), which provides the Minister of Health with independent advice on health and disability issues, contracted the New Zealand Guidelines Group to review the evidence on prostate cancer screening. The guidelines group convened an advisory group consisting of clinical, epidemiological, and consumer representatives, which produced the report *Population-based screening for prostate cancer and testing of asymptomatic men in New Zealand*. The report, which was presented to the NHC in July 2003, concluded that

- the recent rise in the reported incidence of prostate cancer was largely because of the wide use of PSA testing in general practice
- many men, their families, and their whānau were concerned about and asked about prostate cancer
- there was no evidence from randomised controlled trials as to whether or not population screening for prostate cancer reduces mortality and morbidity from the 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 was not supported.

In July 2004 the guidelines group published *Screening for Prostate Cancer—Information for Health Care Practitioners* and *Checking for Prostate Cancer—Information for Men and their Families*. The information guides were based on the earlier report.

Responses to the 2003 report and later information guides (from this inquiry)

Dr Robin Smart told us of his concern that the 2003 report does not reflect the submissions of those who supported screening. He believes that the report and information guides set out all of the negative aspects of screening without mentioning its benefits. We heard that this opinion of the report was held by many urologists and radiation oncologists. Dr Smart told us that he and several colleagues made repeated attempts to persuade the NHC to withdraw or change the report and information guides.

National Health Committee report 2009

In November 2009 the guidelines group produced a report for the Ministry of Health entitled *Cancer Control Strategy Guidance Completion: Update of evidence for prostate-specific antigen (PSA) testing in asymptomatic men*. The Ministry of Health told us it commissioned the report as an updated review of the current evidence from New Zealand and overseas relating to screening for prostate cancer (using PSA), and to ensure best practice in the use of PSA

testing in asymptomatic men (screening). The report concludes that a reduction in mortality and metastases from screening asymptomatic men for prostate cancer has not been proven, and even if it were, several factors would need to be considered before a population-based screening programme would be instigated, including

- the risks of over-diagnosis and over-treatment
- the feasibility of covering the entire population
- whether quality of life would be enhanced or reduced
- the cost-effectiveness of a screening programme.

The report also advises that there is a clear and immediate need for high-quality information in the form of risk calculators and decision-making tools for asymptomatic men and their doctors to use. The information should focus on the individual risk of developing prostate cancer and the risks and benefits of potential treatments if a PSA test is undertaken and found to be positive. The aim of the information is to help men to decide whether to proceed with screening using the PSA test.

Ministry of Health's response to the 2009 report

The Ministry of Health told us that it commissioned the 2009 report in order to use its findings to develop evidence tables to help health professionals and men to assess the benefits and risks of screening. We heard that the review was not intended to provide policy recommendations on screening, but that after considering the report the ministry recommended no change to the existing policy. The ministry told us there is still insufficient evidence for a nationally-coordinated prostate screening programme, but it supports a policy that helps asymptomatic men to make informed choices about screening.

The ministry described the activities that implement its policy. We heard the ministry will work with the Royal New Zealand College of General Practitioners on training GPs to give men and their families balanced information on the benefits and risks of screening. The ministry will support research into the outcomes and side effects of various treatment options for New Zealand men diagnosed with prostate cancer through unorganised screening. The ministry told us that it would continue to watch the two international trials, ERSPC (the European Randomised Study of Screening for Prostate Cancer) and the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial. We heard that the ministry would also continue to monitor the use of PSA testing and patterns of prostate cancer treatment in New Zealand, and then compare these details with international trends.

Prostate cancer rates over time

We were advised that in New Zealand the registration rates of prostate cancer increased gradually over the 1980s and early 1990s particularly with the introduction of PSA testing. New Zealand time-trend data between 1995 and 2005 has shown that the age-standardised incidence rate declined by 22 percent from 121.8 per 100,000 men in 1995 to 95 per 100,000 men in 2005. The age-standardised mortality rate for prostate cancer has declined by 27 percent over the same period from 27.3 per 100,000 men to 19.9 per 100,000 men. The number of PSA tests has increased by 23 percent from 2001 to 2007. Reasons for the declines in both incidence and mortality among New Zealand men are unclear because

modelling, as reported from the United States of America, has not been performed on the New Zealand data to quantify the possible contribution from increased PSA testing.

Figure 3: Prostate cancer registration rate (age-standardised registrations per 100,000) 1998–2008 (Ministry of Health, 2011)

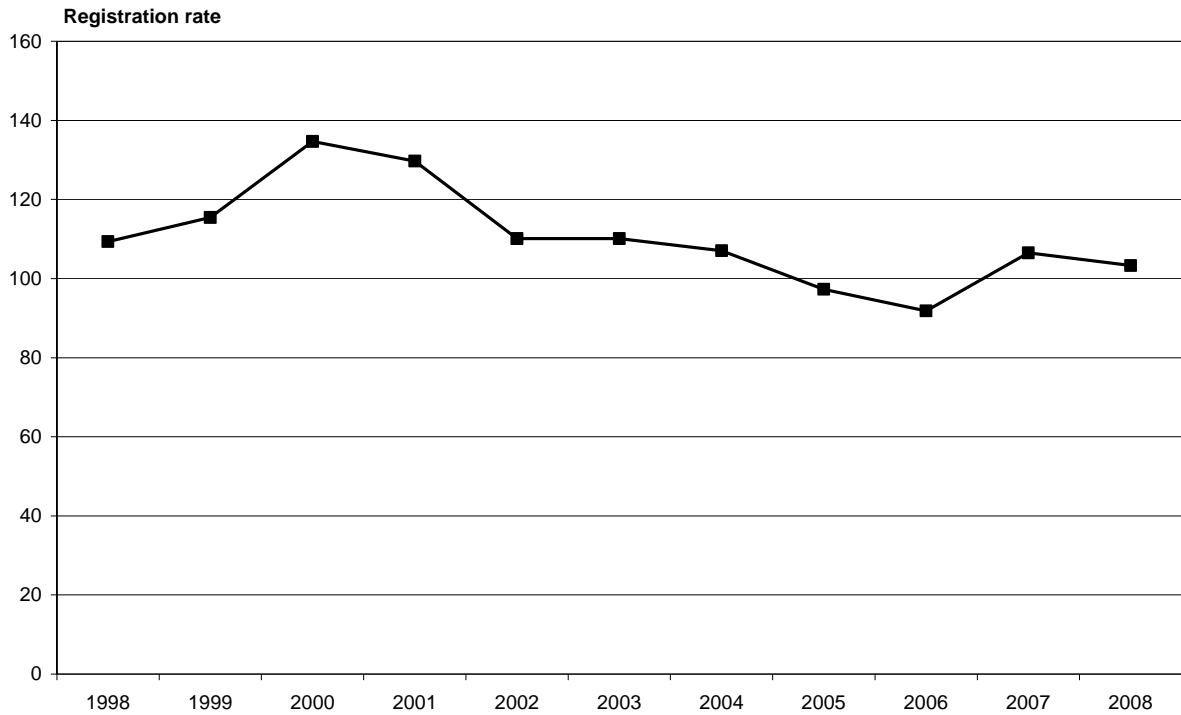
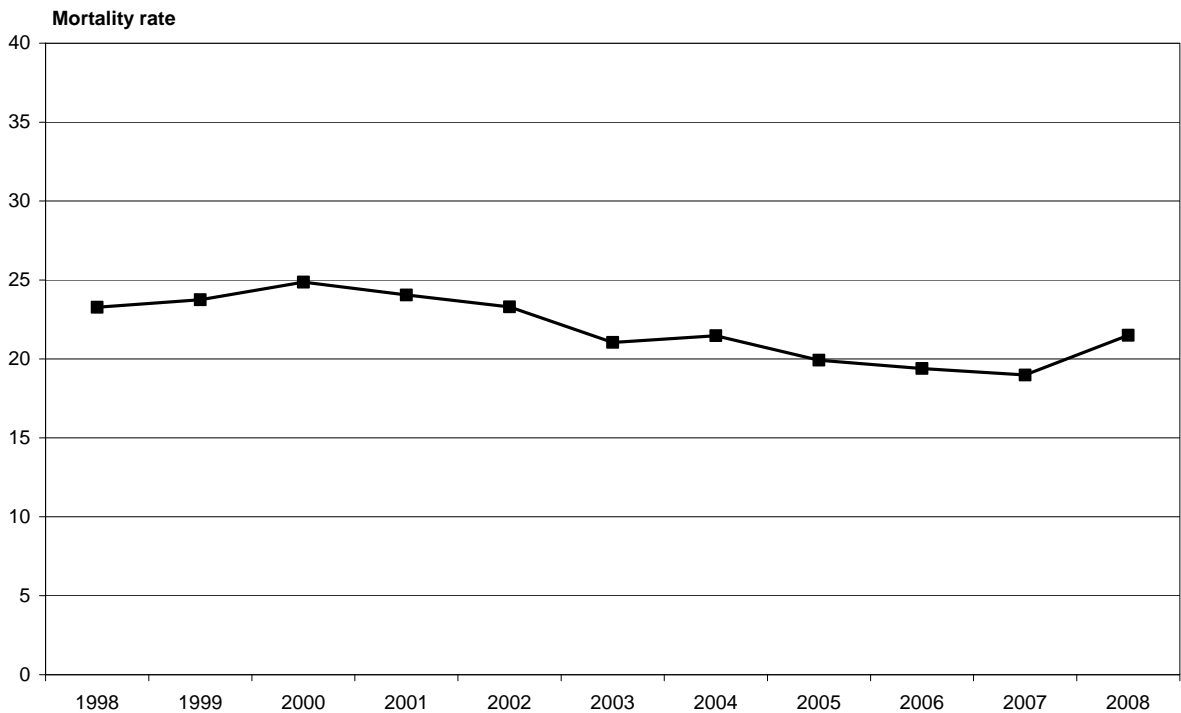


Figure 4: Prostate cancer death rate (age-standardised for 100,000) 1998–2008 (Ministry of Health, 2011)



New Zealand men pay to visit their GPs, but PSA tests are funded by the Government. Within a two-year period, approximately 50 percent of men aged 50 or older will have a PSA test. We understand that the data collected in the New Zealand Health Survey suggests at least 80 percent of the men who undergo the PSA test are asymptomatic. This equates to a 40 percent coverage rate for New Zealand's unorganised prostate cancer screening programme.

Prostate cancer inequities

Inequities and unfair differences are avoidable. Those relating to prostate cancer in New Zealand are significant and worrying but not well understood. We were advised that Māori men experience inequities in access to and quality of diagnosis and treatment. Māori men are about 25 percent less likely to be diagnosed with prostate cancer than non-Māori men, and almost 50 percent more likely to die of prostate cancer. When age and stage of cancer spread at the time of diagnosis are taken into account, Māori men are almost two and a half times more likely to die from prostate cancer than non-Māori men.

The reasons for these inequities are unclear. Māori men may be less likely to get prostate cancer. They may also be more likely to die with undiagnosed prostate cancer because they are less likely to be investigated for the condition and because of their lower life expectancy. The inequities for Māori men relating to prostate cancer are similar to those for most forms of cancer. They are only partially, if at all, attributable to a greater risk of incidence.

We were advised by the Ministry of Health that the inequities for Māori relating to bowel cancer are similar to those for Māori men relating to prostate cancer. The inequities in the risk of death for Māori with bowel cancer are attributable to

- Māori being diagnosed at a later stage
- higher risk of co-morbidity for Māori
- poorer access to, and lower quality of, health care for Māori.¹²

Each of these reasons accounts for about one-third of the increased risk of bowel cancer death for Māori. We understand that an aspect of health-care quality for some Māori men may be the acceptability of testing. We heard that there is evidence of regional differences in access to and quality of treatment for prostate cancer. There may also be access and quality differences relating to socioeconomic position. It is unclear whether, or to what extent, those differences translate into differences in morbidity and mortality from prostate cancer.

Information about health services

We are concerned about the significant gaps in information about the quality and equity of health services for prostate cancer. We were told that research is needed using national data, only some of which is already collected. Progress is being made, however; a joint research initiative funded by the Health Research Council of New Zealand and the Ministry

¹² Sarfati, D., S. Hill, et al. "The effect of comorbidity on the use of adjuvant chemotherapy and survival from colon cancer: a retrospective cohort study", *BMC Cancer* 9:116, 2009.

of Health aims to describe the types of care received by men with prostate cancer. The research will also concentrate on the equity issues, costs, and complications arising from the various types of care, and will determine what proportion of men are likely to undergo biopsy after a PSA test. The results of this research will be available in early 2014. We consider that it should be possible to collate information on the number of men who have a biopsy following PSA testing much earlier than 2014. We consider that this research will be helpful, and were told it needs to be followed by further research on how to solve the problems that it identifies. New systems will have to be tested and implemented. National information and monitoring systems will also need to be developed to ensure continuing quality improvement and quality control.

Improving the quality and equity of care

We consider that New Zealand needs to institute a national quality improvement programme for prostate cancer care and its early detection. To address inequities, all men require access to prostate cancer care. The quality of the care also needs to be improved. We were told that improving access to and the quality of care would also facilitate the creation of an organised prostate cancer screening programme, when the evidence supports its establishment.

We were told groups with an interest in prostate cancer need to work together to assess the current system of access and care, make the necessary changes to ensure that quality care is provided and inequities are addressed, and monitor the system. We understand that this process is likely to take between five and seven years, and would involve the following steps:

- 1 Gathering information from the entire prostate cancer care and screening pathway, identifying costs of care and variations in timeliness, appropriateness, access to and quality of care and outcomes, against minimum standards by region, ethnicity, and age.
- 2 Using the information from step one to determine which areas of the prostate cancer care and screening pathway need improvement.
- 3 Developing and implementing quality improvement measures for the prostate cancer care and screening pathway, for example better information for men and their families and whānau; guidelines for clinicians from discussing screening to testing, biopsy, diagnosis, staging, active surveillance, treatment, and palliative care; systems, data sets, and data collection methods for monitoring; systems for reporting monitoring results back to clinicians and health care providers; systems for ensuring that standards are met when problems are identified. For example access to timely biopsy and specialist assessment in rural areas may require service reconfiguration and additional resources.
- 4 Continuous quality improvement of the prostate cancer care and screening pathway based on repeated rounds of quality assessment.

We consider that five to seven years is far more time than it should take to organise the above.

Recommendations

4 We recommend to the Government that it establish a quality improvement programme relating to the early detection and treatment of prostate cancer. The programme should ensure that all men with prostate cancer have fair access to good quality care (to be achieved within one year).

5 We recommend to the Government that it fund the Ministry of Health to work with non-governmental organisations, groups of patients, and health professionals to set priorities and develop processes to implement a national quality improvement plan for the early detection and treatment of prostate cancer (to be achieved within one year).

6 We recommend to the Government that it continue research into the types of care received by men with diagnosed prostate cancer in New Zealand. The research should include equity issues, costs, and complications arising from types of care, and the proportion of men who undergo biopsy after a PSA test.

4 Early detection of prostate cancer

Barriers to early detection

Men's reluctance to visit the doctor

We heard that many men are reluctant to visit their doctors and often the issues of screening for prostate cancer are not adequately discussed. We are informed that there are many barriers to men seeking advice or care from their GPs, which include

- financial issues
- employment issues
- beliefs and ideologies
- education level
- system issues (such as the variable approach to advice on prostate cancer).¹³

Delays by men in seeking health care can lead to worse outcomes, particularly where treatable conditions become more advanced before treatment is commenced.

Increased access to primary care for men

We believe that men should be encouraged to see a doctor for an annual check-up. We understand that the current national guidelines recommend that all men should visit their GPs for an annual cardiovascular “warrant of fitness” from the age of 45 years, or 10 years earlier if they have known cardiovascular risk factors. From the evidence we have heard, this would be an opportune time for men to be encouraged to discuss the pros and cons of prostate cancer screening.

Inconsistent messages

We were concerned by evidence that men are receiving mixed messages about prostate cancer screening. We were told that the advice is often inconsistent, so that comparing advice from different sources can be confusing and unhelpful. We understand how this confusion has arisen, given the uncertainty in the literature regarding the value of screening for prostate cancer. We were also told that a lack of consistent, clear, accessible information for men and their families is an issue regarding screening and every phase of the prostate care and treatment pathway. There is a clear need for GPs and others involved in this field to have available best-practice, evidence-based tools to help their patients to understand the tests for prostate cancer. This evidence should be up-to-date and easily

¹³ McKinlay, Eileen, *Men and Health: a Literature Review*, Department of General Practice, Wellington School of Medicine and Health Sciences, University of Otago, January 2005.

readable, and have a reference to a website that contains more detailed material (a standard video used in some places around the world would help achieve consistency.) Regular updating would be necessary.

Recommendation

7 We recommend to the Government that it ensure that general practitioners have available best-practice, evidence-based tools to help their patients understand the tests available for early detection and treatment of prostate cancer.

Informed consent

We consider that informed consent is particularly important in relation to prostate cancer screening because of the relatively inconclusive evidence about its benefits, and its potential for well-documented harms, which are often not discussed adequately with men and their families. The Code of Health and Disability Services Consumers' Rights establishes that every consumer has the right to the information that a reasonable consumer in those circumstances would expect to receive: an explanation of the consumer's condition, and of the available treatment options, including an assessment of their expected risks, side effects, benefits, and costs.

Many of the submissions called for men to be given enough information to make an informed decision before choosing or declining to participate in a prostate cancer screening programme. The information requested would cover the benefits of, and harms caused by, screening, as well as more general facts about prostate cancer.

In 2007 the New Zealand Guidelines Group developed a tool for physicians to use to ensure that their patients could give informed consent. The National Screening Advisory Committee told us, however, that the information in the tool is outdated and in fact "inhibitory to providing informed consent".

Recommendation

8 We recommend to the Government that it ensure as many men as possible have access to reliable information on the early detection and treatment of prostate cancer.

Decision-aid

We understand that the National Screening Advisory Committee is developing specifications for a prostate cancer screening decision-aid. A decision-aid is a tool to help people make decisions by giving them information on their options, including that of taking no action, and the probable outcomes of each option, based on evidence, consumer values, and the individual's risk profile. The National Screening Advisory Committee told us that decision-aids improve the decision-making process by improving consumers' understanding of their options. Decision-aids also help health practitioners to provide information in a balanced and accurate way, and would probably solve the problem of mixed messages. We understand the Ministry of Health is deciding who should develop the decision-aid, and how groups with an interest in prostate cancer might be involved in the process. We were told that the decision-aid might be introduced in two to three years' time. We think this should be done within a year.

Recommendation

9 We recommend to the Government that the Ministry of Health develop a prostate cancer screening decision-aid in close consultation with interested parties including the Royal New Zealand College of General Practitioners, the Urological Society of Australia and New Zealand, the Prostate Cancer Foundation of New Zealand, Cancer Control New Zealand, the New Zealand Guidelines Group, the New Zealand Society of Pathologists, and the New Zealand Cancer Society. We consider this should be available within 12 months of this report being presented.

Prostate cancer screening

Screening and the screening pathway

Many of the submissions referred to PSA testing as a screening tool for the early detection of prostate cancer. Screening is defined thus:

A health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatments to reduce the risk of disease or its complications.¹⁴

Screening is more than just the process of questioning or testing, as “it encompasses the whole system or programme of events necessary to achieve risk reduction”.¹⁵ We understand that the screening pathway is a crucial part of a screening programme. It includes the provision of information about the screening test, the results of the screening test, diagnostic testing, and any further assessment or treatment.

Unorganised screening or opportunistic testing

Commentators used a number of terms to describe the current PSA screening practice, including “opportunistic testing” or “proactive testing” to distinguish it from an organised national screening programme. All epidemiologist screening experts agree that PSA testing of asymptomatic men looking for prostate cancer is, by widely accepted definition, screening. Despite the fact that some submitters preferred the term PSA testing, we were told that the correct and widely accepted term remains screening. The Prostate Cancer Foundation, however, prefers to use the term “testing”.

Opportunistic screening is a method of invitation at the initial stage of the screening pathway. A person who is presenting to the health system for another reason is asked a question or offered a test to detect the presence or confirm the absence of a specific condition. Opportunistic screening is a recognised and important method for recruiting people to screening in New Zealand’s two organised screening programmes. It is also the main recruitment method for New Zealand’s unorganised prostate cancer screening programme.

¹⁴ National Health Committee, *Screening to Improve Health in New Zealand*, 2003, p. 2.

¹⁵ Raffle, Angela E, and Gray, J A Muir, *Screening Evidence and Practice*, Oxford University Press, New York, 2009, p. 37.

Unorganised screening programmes are ad hoc and lack quality processes, including monitoring and evaluation. Because of the lack of attendant quality processes, their safety, effectiveness, and cost-effectiveness cannot be assessed or guaranteed.

We understand that unorganised screening means that people are offered tests, delivered to variable standards, and variable systems for ensuring that appropriate interventions and support are offered should the results not be normal. We were concerned to hear about the problems caused by unorganised screening and their effects on men, including the following:

- A lack of quality standards and training resulting in potential exposure of participants to harmful practices, such as investigation or treatment as a result of an unreliable test.
- The lack of national guidance and the resulting risk of over-diagnosis, over-investigation, and over-follow-up because clinicians manage on the side of caution to ensure they do not miss cases.
- Inequity, because those at lowest risk of having the disease may be more likely to be screened: there may also be inequities at any step of the screening programme including invitation, testing, and access to and quality of treatment. Inequities may not be measured or recognised, and actions may not be taken to mitigate them.
- Cost inefficiencies resulting from over-screening, over-investigation, and over-treatment, using resources that could be used elsewhere to gain health benefits.
- Anecdotal submissions that men were overtly dissuaded from a PSA test, or not offered one, rather than being given up-to-date information so that they could make their own choices. The Prostate Cancer Foundation told us they were deeply concerned at the failure to offer prostate cancer testing (or refusal to refer men to seek testing), which may lead to a failure to diagnose prostate cancer until it is too late to be treated effectively, causing unnecessary pain, distress, and death.

Diagnostic tools

We understand that many prostate cancers are slow-growing tumours that occur in older men. Many of these men do not die from prostate cancer, but from other causes. A proportion of prostate cancer tumours are more aggressive, and may grow rapidly and spread to other parts of the body, particularly the bones. The Gleason score, which grades tumours according to typical behaviour, and the PSA level are used to assess who may be at a higher risk of aggressive disease. We heard from Professor Brett Delahunt, a clinical pathologist, that interpretation of the histology by expert pathologists is more reliable now than in the past. We understand that there is conflicting evidence about the usefulness of digital rectal examination (DRE), which is the main examination procedure. Some evidence suggests that DRE does not increase the detection rate in men with PSA above a certain level, and other evidence suggests that prostate cancer detected by DRE is more aggressive than that detected by PSA alone. We were told that the evidence is that DRE does not add much value to PSA testing.

We were told that the PSA and DRE tests are recognised as the best available means of testing for possible prostate cancer. However, we were made aware of research into new methods of testing which may eventually provide clinicians with better diagnostic tools.

Such developments may lead to a change in medical practice and require re-assessment of the desirability of a screening programme.

Recommendation

10 We recommend to the Government that the Ministry of Health continue to assess the advantages and disadvantages of prostate screening on the basis of the latest research and literature.

5 The benefits and harms of prostate cancer screening

The popularity paradox

Most of the submissions we received focussed on the benefits of screening for prostate cancer, with little discussion of the harms. We note that the submissions from screening and public health experts were the most likely to discuss both the benefits and harms of screening, while the submissions from prostate cancer groups were the least likely to discuss the harms. We understand that this is likely to be because of the “popularity paradox.”

We were told the popularity paradox occurs because in most screening programmes some people receive treatment who would never have developed a problem if left unscreened. These people do not realise that they are recipients of over-diagnosis or over-treatment. This is because everybody with a screen-detected abnormality is offered intervention, and there is thus no way of knowing who benefited from the intervention, and who was harmed. Most people treated following screening believe that they have derived major benefit from the process. The greater the incidence of over-diagnosis and over-treatment, the more people there are who believe they owe their health or their lives to the screening programme.

Evidence

We consider that before an organised national screening programme is established there has to be clear evidence that any harm it might cause from over-diagnosis and over-treatment would be outweighed by mortality reduction. We received submissions with a wide range of perspectives on the evidence regarding the benefits of screening for prostate cancer. A number of submissions referred to the results of two studies, the European Randomised Study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

The European Randomised Study of Screening for Prostate Cancer

The ERSPC was undertaken in seven countries in Europe, and involved 162,243 men aged from 55 to 60 years who were screened at intervals of between two and four years. With a median follow-up of nine years, there was a 20 percent relative reduction in risk of death from prostate cancer in men who underwent screening compared with the control group (men who were not in a formal screening programme). The rate of contamination (men in the control group who had PSA testing during the study) was generally low, but variable between countries, ranging from 6.7 percent to 36 percent. The result of this study means that 1,410 men would have to be screened over nine years, and 48 men would need to be treated, in order to prevent one prostate cancer death. The researchers caution that the harms from treatment have yet to be taken into account.

The Prostate, Lung, Colorectal, and Ovarian cancer screening trial

The PLCO cancer screening trial, based in the United States of America, involved 76,693 men aged from 55 to 74 years who were screened at four-yearly intervals. With a median follow-up of 10 years, there was no reduction in risk of death from prostate cancer in men who underwent screening compared with the control group (men who were not in a formal screening programme). The rate of contamination was high at 52 percent. The result of this study indicates that screening did not reduce the risk of death from prostate cancer. The major limitation of this study is that the high rate of screening in the control group means that the study had a low chance of detecting any difference if one existed; however it is possible with longer follow-up that a difference might emerge. It is noted that the screening rate in the US study control group (50 percent) was comparable with the estimated New Zealand screening rate of 40 percent.

Analysis of the evidence

The New Zealand Guidelines Group gave the studies quality ratings using the Graphic Appraisal Tool for Epidemiology. We were told that this widely respected framework evaluates the quality of research publications with respect to internal validity (the lack of bias in the study results), precision, and the applicability of results to practice in New Zealand.

The New Zealand Guidelines Group rated the PLCO study as having poor internal validity, but good precision and applicability, assessing the study as being of good quality overall. The ERSPC was rated as having poor internal validity, good precision, and poor applicability, resulting in an overall rating of poor quality. The only difference in the ratings of the two studies was in their applicability. We were told that the ERSPC was rated as poor-quality because of the flaws in the design, randomisation, and recruitment of subjects in the centres, which was inconsistent. Associate Professor Robert Scragg told us, however, that the New Zealand Guidelines Group erred in rating the ERSPC as being of poor quality. He considers that certain details of the ERSPC, including its larger sample size, mean that it is more likely to have observed a beneficial effect from screening than the PLCO study.

We were most concerned to learn that many well-respected bodies such as the National Cancer Institute in the United States of America regard the PLCO study as having limitations because of the high rate of PSA testing in the control arm.¹⁶ The fact that experienced experts sometimes interpret complex scientific data differently can lead to confusion among lay people. It is extremely important for lay people to have confidence in the experts that interpret the data.

The Göteborg study

We later heard about the Göteborg study, based in Sweden, involving 19,904 men from 50 to 69 years of age. With a median follow-up of 14 years, it indicated a 40 percent relative reduction in risk of death from prostate cancer in men who underwent screening compared with the control group (men who were not in a formal screening programme). The rate of contamination (men in the control group who had PSA testing during the study) was not

¹⁶ <http://www.cancer.gov/ncicancerbulletin/071310/page5>, last accessed 7 July 2011.

reported but was said to be low. The result of this study means that 293 men would have to be screened over 14 years to prevent one death and 12 men would need to be treated to prevent one death from prostate cancer. The researchers caution that the harms from treatment have yet to be taken into account. These results are similar to those which are expected from mammography screening for breast cancer and faecal occult blood testing for bowel cancer. The Göteborg study results need to be confirmed by other studies and the result should take account of the more frequent PSA testing, lower PSA threshold, and the higher rate of prostate biopsies compared with the ERSPC trial. Analysis from this study suggests that most of the benefit occurs after 10 years which means that over time the ERSPC may show a larger benefit, and the PLCO cancer screening trial may also show a benefit with longer follow-up.

Meta-analysis

In September 2010 the British Medical Journal published a meta-analysis of the results of six major randomised trials to determine whether screening using PSA testing reduces prostate cancer mortality. The six trials included the ERSPC, PLCO and Göteborg studies. The meta-analysis found that screening for prostate cancer did not reduce mortality from prostate cancer or overall mortality.

The study did find that screening increased the probability of being diagnosed with prostate cancer by 46 percent and that early-stage prostate cancer was 95 percent more likely to be detected at diagnosis. All of the trials, particularly the older studies, had one or more substantial methodological limitations. No study provided data on quality of life, and information on harms associated with screening was limited.

Table 4: Summary of the key characteristics for the three recently reported randomised studies (BMJ 2010; 341: c4543)

Trial Characteristic	ERSPC	PLCO study	Göteborg study
Trial size	162,243	76,693	19,904
Follow-up duration	9 years	10 years	14 years
PSA cut-off	Variable(3–4 ng/ml)	4 ng/ml	3 ng/ml
Age range	55–69 years	55–74 years	50–69 years
PSA screening interval	2 or 4 years	Yearly	2-yearly
Contamination	Variable (6.7–36.6%)	52%	Details not available (low rate)
Design	Variable regional and local protocols	Single national protocol	Single national protocol
Reduction prostate cancer mortality	20% relative reduction	No reduction	40% relative reduction
Absolute benefit	0.71/1000 men	Not applicable	3.4/1000 men
Numbers needed to treat to prevent one death	1/48 men	Not applicable	1/12 men

The clinicians' perspective

During the hearings for this inquiry, we heard that the Urological Society of Australia and New Zealand (USANZ) has recently revised its policy and recommendations about screening for prostate cancer, in the light of the PLCO and ERSPC studies, and it has communicated these revisions to doctors in Australia and New Zealand. The society told us that while it does not advocate population-based screening, it considers that there is sufficient evidence that an earlier diagnosis of prostate cancer will reduce the risk of death from the disease. It concludes that a combined PSA and DRE test offers men between 55 and 69 years of age a 20 to 30 percent reduction in cancer mortality.

USANZ recommends that men should have their first PSA test at 40 years of age, rather than 50, to allow each man's risk of getting prostate cancer to be assessed. A higher than median test-score for men of this age indicates a future risk three times the normal, over a ten- to 20-year period. USANZ considers that this initial test would identify those at greater risk, and hopefully prevent over-treatment and at the same time reduce the chance of men dying in their 50s and 60s. However, any man with a familial risk should be monitored from the age of 40 onwards.

USANZ said that men with passive forms of prostate cancer already have the option of being managed in the short to medium term with "active surveillance", which involves regular PSA tests and DRE at appropriate intervals. If the cancer is suspected to be advancing, then trans-rectal ultrasound and sector biopsies are performed. Curative treatments are recommended only if the cancer is actually advancing; otherwise, men live with their cancer. Although active surveillance is not for everyone, it has the major advantage of avoiding side effects from treatment. More importantly, the society is concerned that some men are still being told not to bother having the PSA and DRE tests, and doctors may still decide not to offer them.

USANZ published a statement on 2 June 2011:

The level of risk a man faces of dying from prostate cancer can be predicted from a single prostate specific antigen (PSA) test taken before 50 years of age, according to a study recently presented at the American Urological Association (AUA) Annual Washington meeting.

The evidence now appears overwhelming that men in their 40s need to speak with their GPs about the merits of undertaking an early PSA test rather than waiting. For most this simple blood test and examination will provide peace of mind. For others it will result in closer surveillance and much greater opportunity for early detection and treatment.¹⁷

The Prostate Cancer Trials Unit at the University of Otago told us it believes there is evidence that PSA testing can provide survival advantages for asymptomatic men aged between 50 and 70 years. The unit considers that a significant proportion of the approximately 600 New Zealand men who die of prostate cancer each year might be saved

¹⁷ <http://www.usanz.org.au/uploads/29168/ufiles/110602EarlyTestingMediaRelease.pdf>, last accessed 23 June 2011.

if their disease were diagnosed at an earlier stage. We heard that the different results in the PLCO trial and the ERSPC are likely to reflect the unorganised screening practices in the US population, and the contamination of the PLCO study's control group during the observation period.

The unit recommends that

- all men aged 50 to 70 years be encouraged to have a PSA test every four years
- men who have one or more first-degree relatives who have been diagnosed with prostate cancer have an annual PSA test from the age of 50 to the age of 70
- men older than 70 who have never had a PSA test have the option of having one performed, but that they be informed that a prostate cancer often does not need treatment
- men from ethnic minorities, especially Māori, and men in lower socio-economic groups be targeted for education campaigns on the value of screening.

The British Journal of Urology International published an article in April 2008 relating to the Tyrol area of Austria, and known as the “Tyrol Prostate Cancer Demonstration Project: Early Detection, Treatment, Outcome, Incidence, and Mortality”. The objective was to evaluate the effectiveness of a well-controlled programme of early detection and treatment of prostate cancer in the population of Tyrol, where such a programme of early detection and treatment was initiated in 1988, and where PSA testing was offered free to all men aged 47 to 75 years from 1993. While it was not a randomised prospective controlled study it contains useful information to inform practice in New Zealand.

The results showed that “in all, 85.6% of eligible men have been tested at least once since 1993. Cancer deaths in Tyrol were 54% lower than expected compared with 29% in the rest of Austria.” The decreasing trend in prostate cancer mortality was significantly greater in Tyrol compared with the rest of Austria ($p=0.001$). A significant migration to lower-stage disease occurred and radical prostatectomy was associated with low morbidity.

The public health (epidemiological) perspective

We were told that public health experts are interested in the balance of harms and benefits for the whole population. The public health perspective involves a desire to protect the population from harm if there is no proof of the benefits outweighing the harms. We heard from epidemiologists from the University of Otago, who estimated that at least 50 percent of prostate cancer that is diagnosed would not have caused illness during a man's lifetime and therefore did not need treatment. These men undergo unnecessary treatment, with associated morbidity such as chronic impotence and incontinence. The submission emphasised that men need to be adequately informed about the risks and benefits of screening, and that the information should not be based on the clinician's belief system.

We were also told that no international organisations involved in cancer control support the establishment of a population-based screening programme, and that the submitters do not support screening for prostate cancer. One submitter argued that the amount of screening should be reduced, because the evidence of benefit over harm remains insufficient.

Recommendations

11 We recommend to the Government that the Ministry of Health continue to monitor international trials relating to the benefits and harms of prostate cancer screening. When new evidence arises, the Ministry of Health should update its policies on screening and prostate cancer.

12 We recommend to the Government that the Ministry of Health endeavour to decrease any harms caused by unorganised prostate cancer screening.

13 We recommend to the Government that it support continued research into the early diagnosis and treatment of prostate cancer.

Summary of harms from screening and investigation

There are minimal risks directly attributable to PSA testing or to the transrectal ultrasound (TRUS) biopsy. The significant harms are those from prostate cancer treatment, and they are of particular concern when treatment complications are a consequence of over-diagnosis and over-treatment. Reports on the psychological impacts of prostate cancer diagnosis and treatment are limited.

Studies reporting complications from TRUS biopsy show that it is a very safe procedure, with the common complications of rectal pain, rectal bleeding, urinary bleeding, and infection being transient and self-limiting. The risk of serious complications from TRUS biopsy such as severe infection, major bleeding, or urinary retention requiring hospital admission occur in less than 2 percent of subjects.

Cost-benefit analysis

We received few submissions on the costs and benefits of prostate cancer screening and prostate cancer treatment. A number of submissions raised concerns about the health system's capacity to deal with an increase in screening. We consider that information needs to be gathered to clarify the costs of diagnosing and treating prostate cancer in New Zealand. We expect that further results from the ERSPC and the PLCO trial will provide reliable evidence on the possible mortality reduction and the harms produced by screening. A cost-benefit analysis of organised prostate cancer screening in New Zealand could be undertaken once the benefits and harms of prostate cancer screening are established, depending on whether the benefits are found to outweigh the harms.

Recommendations

14 We recommend to the Government that it undertake an analysis of the costs of the current unorganised prostate cancer screening in New Zealand.

15 We recommend to the Government that it undertake a costing of a quality improvement programme for prostate cancer diagnosis and treatment, which should include the development of consumer information for men and their families; the analysis of current service delivery; the development and implementation of guidelines; and the development and implementation of national monitoring indicators.

6 Treatment of prostate cancer

Treatment options

The established treatment options for prostate cancer are radical prostatectomy, hormone therapy, external beam radiotherapy, and high-dose-rate brachytherapy, all of which are available through the public health system. We understand that many newer treatments are only available privately, including low-dose-rate permanent seed implant radiotherapy (low-dose-rate brachytherapy), cryotherapy, intensity-focussed ultrasound, and robotic surgery.

We were told that there is little national data available regarding the timeliness, appropriateness, quality, and equity of New Zealand prostate cancer treatment. If national monitoring of prostate cancer management were established, we consider that this data should be collected and analysed.

Active surveillance

Active surveillance is a way of managing men with low-risk prostate cancer. It involves monitoring the course of the disease, with the aim of intervening if the cancer progresses. Patients under active surveillance undergo a regular schedule of follow-ups including a prostate exam, PSA tests, and repeated needle biopsies.

There is no New Zealand data on the proportion of men being offered or accepting active surveillance as a management option for their prostate cancer. Although active surveillance is advocated in the USA and many other countries as a reasonable strategy for many men with low-risk prostate cancer, data from the USA from 1990 to 2006 indicates that active surveillance is used in less than 10 percent of men with prostate cancer.¹⁸ It is estimated that 25 to 50 percent of men who begin active surveillance receive some form of treatment within five to 10 years, and that up to half of these treatments are because of patient choice rather than clinical progression of disease.¹⁹ We have been told that active surveillance is now used more commonly. Further randomised studies will assist in informing future practice.

Treatment morbidity

There is disagreement about the amount of harm, or morbidity, caused by the side effects of treatments for prostate cancer. Such side effects include erection difficulties, urinary problems, and bowel problems, and incontinence. The impact of these side effects on quality of life, particularly in younger men, and the potential for over-treatment and resulting morbidity, have been given as reasons why epidemiologists do not support either screening or opportunistic testing for prostate cancer. These risks need to be balanced

¹⁸ Dall'Era, MA, Konety, BR, et al., "Active surveillance for the management of prostate cancer in a contemporary cohort", *Cancer* 112 (12), 2008, pp. 2664–70.

¹⁹ Carter, HB, Ketterman, A, et al., "Expectant management of prostate cancer with curative intent: an update of a Johns Hopkins experience", *J Urol*, 178 (6), 2007, pp. 2359–64, pp. 64–5; Klotz, L, "Active surveillance for favourable risk prostate cancer: what are the results, and how safe is it?", *Semin Radiat Oncol*, 18 (1), 2008, pp. 2–6.

against the risk of dying from prostate cancer or suffering distressing symptoms from its spread. Appendix C is a summary of the harms caused by treatment.

Countering this view, the Urological Society of Australia and New Zealand explained that outcomes as regards erectile dysfunction have improved significantly in the past 10 years, and that early detection allows nerve-preserving surgery to be performed, so that 80 to 90 percent of pre-treatment erectile status can be retained. Brachytherapy allows similar preservation. The USANZ also said that data citing incontinence levels of 30 percent is no longer correct, and the percentage has decreased to less than 5 percent.

The society reiterated that earlier detection allows less invasive treatment to be used, meaning fewer side effects and better outcomes. It held the view that harms have been over-emphasised, and the over-treatment effect overstated. It was important for GPs to provide the best and most up-to-date information to their patients, to help them make good decisions.

We are very aware of the effect that significant continuing side effects can have on a man's quality of life. Long-term incontinence of bladder or bowel and sexual dysfunction are significant issues. The Senate Select Committee on Men's Health reported that men often need psychological support to deal with these side effects of treatment, and we would encourage the Government to make provision for such support.

Recommendations

16 We recommend to the Government that it require the Ministry of Health to establish national monitoring of prostate cancer management and analyse the data that it collects on an ongoing basis.

17 We recommend to the Government that it require the Ministry of Health to facilitate research into the side effects of investigative procedures such as Transrectal Ultrasound Guided biopsies, and into definitive treatment in the New Zealand context.

7 Men's health and improving prostate cancer treatment quality and equity

Men's health

One theme that emerged during the hearings and from the written submissions was that prostate cancer screening was increasingly being viewed as the flagship for an emerging men's health movement. There would be many aspects of a prostate cancer treatment quality and equity improvement programmes which could help support and promote men's health. For example, an informed consent decision-aid could be developed in collaboration with men's health advocacy groups, who could then be contracted to promote and help monitor the use of the decision-aid.

We also consider that organisations involved in key men's health issues such as smoking cessation, diabetes prevention and control, sexual health, mental health, and cardiovascular risk factor screening, could be encouraged to work with men's health advocacy groups, men's health researchers, and the Ministry of Health on ways of addressing a core set of men's health issues, including prostate cancer, in a collaborative and coordinated way. This approach could be used to involve key groups in the development and implementation of a quality and equity improvement plan for prostate cancer screening.

Quality and equity improvement programme

Submitters recognised the need to improve all stages of the current pathway of screening including information, informed consent, testing, diagnosis and treatment, including treatment for incurable prostate cancer. In particular, submitters recommended that

- the quality of existing services from informed consent through to follow-up after treatment be improved
- inequities of access to and the quality of existing services from informed consent through to follow up after treatment be improved
- data collection and reporting of current management practices be improved
- there be support for research on current and future approaches to the diagnosis and treatment of prostate cancer.

We were advised that establishing a national approach to quality and equity improvement for diagnosing and managing prostate cancer could reduce the potential harm from unorganised screening. Further, a national prostate cancer quality and equity improvement plan could help establish a sound foundation for a future organised screening programme.

An overarching national approach to prostate cancer risk and quality improvement could be achieved by

- monitoring by the Ministry of Health of reports from international randomised trials on the benefits and harms of prostate cancer screening

- developing and providing better information for men and clinicians, including a decision-aid tool on PSA screening
- assessing the cost of providing the current levels of service to New Zealand men with prostate cancer by the Ministry of Health
- implementing incremental changes to improve the quality of the prostate cancer diagnosis and treatment pathway, developing consumer information for men and their families, analysing current service delivery, developing and implementing guidelines, and of national monitoring indicators
- researching prostate cancer inequities and exploring the outcomes from current care, including harms of treatment.

Implementing a coherent national approach to quality improvement will require better collaboration and understanding between key interest groups involved with prostate cancer and men's health.

8 Conclusion

Submissions to our inquiry expressed a wide range of views on prostate cancer screening regarding all stages of the continuum of care from prevention, screening, and treatment of early cancer, to the management of men with incurable prostate cancer. Submitters represented key interest groups including those directly affected by prostate cancer, community groups, prostate cancer lobby groups, and screening and health experts.

Five major themes emerged from the submissions; the first four we have discussed in detail in our report, while issues of cost-effectiveness cannot be considered fully until further evidence of the benefits and harms from the clinical studies on prostate screening becomes available.

The key themes of the submissions were

- quality and equity improvement along the existing unorganised prostate cancer screening pathway
- perceived benefits of prostate cancer screening
- perceived harms from prostate cancer screening
- arguments for and against establishing an organised prostate cancer screening programme
- cost-effectiveness of screening for prostate cancer.

Prostate cancer is a significant public health issue, and submitters recognised the need to improve the current pathway of screening, including information, informed consent, testing, diagnosis, and treatment, including treatment for incurable prostate cancer. In particular, submitters recommended that

- the quality of existing services be improved
- inequities of access to and the quality of existing services be improved
- data collection and reporting of current management practices be improved
- support be provided for research on approaches to the diagnosis and treatment of prostate cancer.

There was a wide range of perspectives on prostate cancer screening, including different understandings of what constitutes screening. It is evident that current practice in New Zealand involves a large unorganised screening programme, with at least 40 percent of men 50 years or older having a PSA screening test. Unorganised screening is accessible in various ways to men who have not previously been diagnosed with prostate cancer; and where it is deemed necessary, it is followed by further investigation and treatment with the aim of reducing death from prostate cancer.

Regardless of their views as to whether screening should take place at all, groups of submitters recognised the need to improve the current unorganised prostate cancer screening and care pathway.

If an organised national screening programme is to be established there has to be clear evidence that the mortality reduction outweighs the harms from over-diagnosis and over-treatment. Submissions provided a wide range of perspectives on interpretation of the evidence of the benefits and risks. From the evidence presented it can be concluded that there may be improvements in mortality from prostate cancer screening, but it is less certain whether this benefit justifies the risk of harms and the costs. The justification for a nationally organised screening programme remains uncertain. What is clear is that there is a significant need for an organised approach to decreasing the harm from unorganised screening, particularly by improving the quality and equity of care for men under investigation for and diagnosed with screening-detected prostate cancer.

Until there is evidence in favour of the establishment of an organised prostate cancer screening programme, the approach to unorganised screening remains problematic. However, most submissions agreed that men should have access to high-quality information and support to make informed decisions about screening. The provision of information about prostate cancer screening could be included in a broader men's health programme.

The two international randomised trials have not yet resolved the controversy as to whether there should be a nationally organised screening programme for prostate cancer. Until more definitive results are available from the trials, or until a better prostate cancer screening test is developed, the decision on screening for prostate cancer is a difficult choice for men and those close to them. Men undergoing screening need to be provided with clear, consistent information to inform their decisions. Results from the inquiry indicated that men are receiving mixed and confusing messages about screening for prostate cancer.

Submitters noted that there is little consistency of advice and that advice from different sources can be in conflict. The varying approaches of primary health care practitioners when providing information to men was viewed as a significant problem. Many submitters called for better information, decision support tools, and education of health practitioners. In particular submitters noted that, as well as the specific requirement for better-informed consent, men need better information about prostate cancer and screening for prostate cancer in general, and men and their families require good information to help them make decisions at every point on the screening pathway.

A small number of submissions addressed the issue of the cost of prostate cancer screening for New Zealand's health system. There is no readily available information to assess the cost of current unorganised prostate cancer screening in New Zealand. Further, it is unclear what the costs are of such screening in New Zealand. Hence the additional costs of an increase in demand for unorganised screening are unknown. A cost-effectiveness analysis of prostate cancer screening cannot be done until basic information on such screening becomes available. At a minimum more conclusive information is required on the possible benefits, and basic information is required on the harms, particularly from over-diagnosis and over-treatment. Further results from the European and US randomised

controlled trials are likely to provide information necessary for a cost-effectiveness analysis of prostate cancer screening in New Zealand. Research into the likely costs of screening for prostate cancer in New Zealand would also be required for a cost-effectiveness analysis.

Establishing a national approach to improving quality and equity in diagnosing and managing prostate cancer has the potential to reduce the significant harm which is likely to arise from unorganised screening. Further, a national prostate cancer quality and equity improvement plan could help establish a sound foundation for an organised screening programme in the future.

Appendix A

Committee procedure

The committee called for public submissions on the inquiry. The closing date for submissions was 21 August 2009. The committee received 29 submissions from the organisations and individuals listed in Appendix B and the committee heard 16 of the submissions orally.

Committee members

Dr Paul Hutchison (Chairperson)

Chris Auchinvole (from 9 June 2011)

Dr Jackie Blue

Hon Ruth Dyson (until 9 February 2011)

Kris Faafoi (from 9 February 2011)

Kevin Hague

Hon Luamanuvao Winnie Laban (until 13 October 2010)

Iain Lees-Galloway

Hon Damien O'Connor (from 13 October 2010 until 9 February 2011)

Grant Robertson (from 9 February 2011)

Eric Roy

Nicky Wagner

Michael Woodhouse (until 9 June 2011)

Advisers

Dr John Childs, Ministry of Health

Dr Nina Scott, Ministry of Health

Associate Professor Robert Scragg

Appendix B

List of submitters

John H. (Doc) Mountain
Kerry Martin
Patients Rights Advocacy Waikato
Noeline Lofthouse
Professors D S Lamb and B Delahunt
Mr Robin Smart
Prostate Cancer Foundation of New Zealand
Rural Women New Zealand
Morell Metcalfe
Duncan and Eleanore McLean
Kim Cook
The Royal New Zealand Returned and Services Association
Cancer Society of New Zealand
Anita Walker and the “Healthy Nuts”
Mark and Eileen von Dadelszen
Associate Professor Brian Cox and Dr Mary Jane Sneyd
The Royal New Zealand College of General Practitioners
Urological Society of Australia and New Zealand
Alta Whiting, ’Tunisi ’Efoti, Lenore Smith, and Sesimani Ngata
Terrence G Story
National Advisory Committee on Health and Disability
Richard Quinn
Ross Lawrenson and Jim Vause on behalf of the National Screening Advisory Committee
New Zealand Guidelines Group Incorporated
Dr Lannes Johnson
David G Chamberlain
John Forman, New Zealand Organisation for Rare Disorders
David Walpole
Cancer Control New Zealand

Appendix C

Summary of harms from treatment

Surgical prostatectomy and radiotherapy techniques can all cause complications; however some data suggests that newer techniques may reduce the risk of some complications. Prostatectomy has higher risks than radiation therapy of causing short-term urinary incontinence and sexual dysfunction; however the risk of longer-term sexual dysfunction may be similar. Radiation treatment has a higher risk of short- and long-term bowel side effects than surgery. Among the radiation options, conventional external beam radiotherapy such as 3D conformal radiotherapy and intensity-modulated radiation treatment (IMRT) have a higher risk of bowel complications compared with brachytherapy. The data on newer techniques such as IMRT and robotic-assisted prostatectomy are too preliminary to make definitive conclusions about the overall complication risks.

The main complications of surgical prostatectomy are

- perioperative mortality
- major and minor procedure-related complications (such as bowel injury)
- urethral stricture
- acute (within 3 months) and late (after 12 months or more) urinary incontinence
- acute and late erectile dysfunction.

There are many case series and reviews published since 2003 on the risks associated with radical prostatectomy, but good-quality studies on comparison of harms across the different surgical approaches are limited. Most of the comparisons can be made only indirectly, using studies of different patient groups with differing clinical characteristics and approaches to measurement of the complications. The recent studies continue to produce a wide range of estimates with a significant degree of overlap between surgical approaches. A summary of the data is presented in table 5.

Mortality from prostatectomy is rare, reported at less than 1 percent, and major post-operative complications such as haemorrhage, deep venous thrombosis and cardiovascular events are uncommon; they are estimated to occur in 3 to 4 percent of men. Minor complications such as infection, transient bowel problems, and blood loss have been estimated to occur in up to 8 or 9 percent of men. Reported post-operative complications vary widely and depend on surgeons' experience, patient factors, the extent of the cancer, and the type of prostatectomy procedure.

There is a wide range of risk reported for short- and longer-term complications from prostatectomy. Reported rates of urethral stricture vary from less than 1 percent to 15 percent. However, more recent studies suggest that the risk of stricture has declined over time with improved prostatectomy procedures.

Table 5 Estimates of short- and long-term complications from surgery²⁰

Complication	Risk estimate	Comment
Urethral stricture	0–15%	Evidence shows rates have declined over time with evolving surgical techniques. Pooled-rate early studies 5.3% Pooled rate since 2005 1.7%.
Urinary incontinence (short term)	8–65%	There is wide variation across studies. Comparisons across surgical approaches are difficult to evaluate. For most men this resolves within 12 months.
Urinary incontinence (longer term)	5–15%	Variable rates and severity of incontinence at 12 to 24 months. Longer term difficult to evaluate.
Erectile dysfunction (short term)	50–90%	First 3 months after surgery.
Erectile dysfunction (long term)	50–90%	Wide-range data indicates that long-term rates are lower following nerve-sparing procedure. Nerve sparing estimate 30–50% Results often complicated by use of hormone therapy.

Short-term urinary incontinence remains a significant problem following radical prostatectomy, regardless of surgical approach. Up to 40 percent of patients are reported to have incontinence at three months post-surgery. However, for many men this will be minor and it resolves for most men twelve or more months after surgery. Reports show that 5 to 15 percent of men will require occasional or consistent use of a pad longer term.

Short- and long-term erectile dysfunction (impotence) remains a significant concern for men undergoing radical prostatectomy, regardless of approach. Up to 70 percent of men may experience erectile dysfunction in the first three months following surgery, however this improves over the first 12 months. Between 30 and 50 percent of men who were potent before bilateral nerve-sparing surgery will have erectile dysfunction 12 months after surgery; however the estimated risk for erectile dysfunction following non-nerve-sparing

²⁰ <http://www.icer-review.org/index.php/mgmtoptionlrpc.html>, last accessed 8 July 2011.

surgery is 50 to 80 percent. Other aspects such as libido and orgasm are not affected by surgery and many men can be helped with the range of drugs commonly used for treatment of erectile impotence.

The main complications from radiation treatment are as follows:

Acute effects (these are transient and usually resolve within 6 weeks of completing treatment)

- bowel symptoms
- bladder symptoms
- other general effects (such as skin reaction and fatigue).

Late complications (these develop after three months and may be progressive)

- altered bowel habit including incontinence
- persistent urinary symptoms
- erectile dysfunction (impotence).

Second malignancy

A summary of radiation complications is provided in table 6.

Table 6 Short- and long-term complications from radiotherapy²¹

Complication	External beam (3D CRT)	IMRT	Brachytherapy
Bowel complications (short term)	Not assessed	3–50%	0–10%
Bowel complications (long term)	10–21%	1.6–24%	0–13%
Urinary complications (short term)	Not assessed	6.9–49%	5%–10%
Urinary complications (long term)	8–23%	6–23%	0–40%
Erectile dysfunction (long term)	28–39%	48–49%	14–43%

The risk and severity of late effects from radiation treatment reported in recent studies are difficult to evaluate because of the widely varying populations and study methodologies. The acute (early) side effects from radiation are usually of minor intensity but a small proportion of men will have more significant acute complications. The long-term effects of radiation treatment are of more concern. The reports on erectile dysfunction are of variable

²¹ <http://www.annals.org/content/early/2011/06/03/0003-4819-155-3-201108020-00347.full>, last accessed 18 July 2011.

quality, and it may be similar to those for nerve-sparing prostatectomy, with an estimated rate of 30 to 45 percent at two years following treatment. Reports suggest that brachytherapy erectile failure may respond well to drugs that are commonly used to treat erectile impotence from other causes.

Significant bowel complications are reported in about 5 to 15 percent of men and appear to be higher following conventional external beam radiotherapy (3D CRT) and IMRT approaches than after brachytherapy. However, firm conclusions cannot be drawn about the advantages of IMRT or brachytherapy compared with conventional external beam radiotherapy because of limited comparative evidence.

The risk of second malignancy from radiation treatment is estimated at 0.5 to 1 percent. The option of prostatectomy is relevant for younger men, to reduce the risk of second malignancy.

Although there have been early reports of quality of life data from the ERSPC and PLCO trials indicate that their results are consistent with more recent evidence. It is expected that further information on treatment harms and the impact on quality of life will be reported from these two studies. At present there is still insufficient evidence to assess whether the potential benefits reported in the ERSPC and Göteborg studies outweigh the harms. However, many clinicians and men believe that the evidence of benefit outweighs the harms. The current evidence means that adverse effects associated with treatment options should be discussed individually with men, and should be weighed alongside the relative risk of mortality and of problems from advanced disease.