NATIONAL CANCER PREVENTION POLICY

2004–06

Screening to detect cancer early

Prostate cancer

The Cancer Council Australia

Prostate cancer

The current evidence does not support population screening of well men for prostate cancer. Individual men who decide to be tested should be able to do so on the basis of informed consent, having access to full information about the potential benefits and risks associated with testing.

Prostate cancer in Australia

In 2000, prostate cancer was the most common cancer (apart from non-melanoma skin cancer) diagnosed in Australian men, with 10,512 new cases diagnosed (AIHW & AACR 2003).

Prostate cancer mainly affects men in older age groups. Over 85% of new cases and over 96% of deaths occur in men over sixty years. It is rare in men under forty-five years of age. Although the incidence of prostate cancer increases with age, the threat to life from prostate cancer decreases with age. This is because the disease generally develops slowly. Men older than seventy-five years or with less than ten years life expectancy are thought to be least at risk from a diagnosis of prostate cancer. Men fifty to seventy-five years of age are at greater risk. However, irrespective of the risk it poses, a diagnosis of prostate cancer at any age can have a major impact on a man's quality of life.

The reported incidence of prostate cancer was relatively stable until 1989 but between 1990 and 1994 there was a dramatic rise in the number of new cases of prostate cancer registered in Australia (AIHW & AACR 2002a). This has been attributed to increased detection of the disease through increased investigations, particularly the use of prostate-specific antigen (PSA) testing (AIHW & AACR 2002a); see discussion below in 'Tests for prostate cancer'.

Following a peak between 1994 and 1997, the age-standardised prostate cancer incidence rate fell by 30%, then stabilised in 1998 and 2000 (AIHW & AACR 2003).

A further measure in assessing the impact of prostate cancer is survival: the proportion of patients still alive at a given time after their cancer diagnosis. This rate is greatly influenced by the lead-time effect of earlier diagnosis. In Australia the reported five-year relative survival ratio (a measure which allows for the risks of death from other causes) for men diagnosed with prostate cancer increased from 59.3% in 1982–86 to 82.7% in 1992–97 (AIHW & AACR 2002b).

The mortality rate from prostate cancer, which is significantly lower than the incidence rate, is declining in many Western countries. In Australia, the rate decreased by 1.3% per annum between 1990 and 2000 (AIHW & AACR 2003). The burden of prostate cancer is likely to increase with the ageing of the Australian population, and this has major public health and economic implications (Weller et al. 1998).

Can prostate cancer be prevented?

The causes of prostate cancer are poorly understood. Geographical and racial differences in rates of prostate cancer provide compelling evidence that environmental and lifestyle factors are involved (Weller et al. 1998). Age and family history are the strongest risk factors in Australia. Researchers continue to examine other possible risk factors, including diet, weight and physical activity. An effective approach to primary prevention of prostate cancer has not yet been identified (Harris & Lohr 2002).

Chemoprevention has attracted considerable attention, but is not yet ready for routine use. A factorial randomised trial examining selenium and vitamin E is in progress (Klein 2003). A randomised trial of finasteride, an inhibitor of 5alpha-reductase (which inhibits the conversion of testosterone to dihydrotestosterone, the primary androgen in the prostate) found an overall reduction of prostate cancer incidence, but at the cost of considerable side effects and a higher incidence of high grade cancers (Thompson et al. 2003). This approach is not recommended.

As well as identifying primary risk factors, research seeks to identify other factors to assist in defining target groups for screening. However, an Australian review noted that there are no epidemiological data that define risk groups sufficiently for targeted screening activities (Weller et al. 1998). The possible exception is men with a strong family history of prostate cancer. Men with a family history in a first-degree relative have a two-and-a-half times greater risk, with some evidence that the risk is higher if the relative was diagnosed before the age of sixty years (Johns & Houlston 2003). The genetic basis has not been identified, though men carrying mutations of the breast cancer susceptibility genes BRCA1 or BRCA2 gene have an increased risk of several types of cancer including prostate cancer (Liede et al. 2000). The questions of whether, when and how often such people should be monitored have yet to be addressed.

Tests for prostate cancer

Prostate-specific antigen test

The prostate-specific antigen (PSA) test is commonly done to try to detect prostate cancer. It measures the amount of PSA in blood, since virtually all PSA is produced by the prostate gland. PSA levels can be raised due to a range of conditions and, depending on the PSA level, as many as two-thirds of all cases of elevated PSA will be due to a non-cancerous condition (USPSTF 1996). The level of PSA used to justify biopsy is commonly set at 4 ng/ml. However, since cancer may be present with lower levels (Babaian et al. 2001) some have advocated a cut-off of 2.5 ng/ml (Punglia et al. 2003). Increased sensitivity by use of a lower level will decrease specificity, leading to a higher rate of unnecessary biopsies, and an increase in over-diagnosis (see below).

Accuracy may be improved by taking into account a man's age, since PSA levels increase with age due to benign enlargement of the prostate. It may also be improved by measuring the proportion of free to total or complexed PSA, since men with prostate cancer tend to have lower levels of free PSA than men who don't have prostate cancer. However, there is no consensus yet on either of these measurements (Harris & Lohr 2002; Stenman 1997).

Digital rectal examination

Another form of testing is digital rectal examination (DRE). This test involves manual examination of the prostate gland through the rectum. Some abnormalities may be felt but it is not possible

to feel all the prostate. A cancer that is in part of the prostate gland out of the doctor's reach, estimated to be 25–35% of the prostate, may be missed (USPSTF 1996). In addition, small (stage A or T1) cancers cannot be felt. Wide variations in reporting occur between doctors (AHTAC 1996).

Transrectal ultrasound and biopsy

Neither the PSA test nor DRE, either alone or together, is a truly accurate test for prostate cancer. If abnormalities are detected by a PSA test or DRE, patients will need further investigations to confirm a diagnosis of prostate cancer. Other tests available are a transrectal ultrasound (TRUS) and biopsy. The TRUS gives an image of the prostate and assists accurate needle biopsy of the gland. The needle biopsy involves six or more samples of tissue being removed for examination under the microscope. Even though tissue is taken from a number of locations, and most malignant cancers will be detected, it is not possible to say with complete certainty that a negative result means that there is no cancer present. The test carries risks of infection and bleeding (AHTAC 1996).

The sensitivity and specificity of the screening tests in use for prostate cancer cannot be determined with certainty (i.e. confirmed by pathology tests on tissue samples) because biopsies are generally not done on people with negative screening tests (USPSTF 1996). Only the positive predictive value —the probability of cancer when the test is positive—can be calculated with any confidence, but this also is subject to methodological difficulties from the needle biopsy measurement (USPSTF 1996).

There is no single test or combination of techniques that can detect prostate cancer and predict which cancers, if left untreated, are likely to:

- result in few if any symptoms, require no treatment and have no effect on life expectancy
- progress to a stage of widespread and aggressive cancer.

Most recent research has focused on the PSA test, particularly refinements to improve the sensitivity and specificity of the test. Various derived measures, including free-to-total PSA ratio, PSA density and age-specific ranges, have been suggested (Bangma et al. 1995) but have not become established as superior to total PSA (Ciatto et al. 2001). The question remains whether measurement of PSA provides benefits to patients in terms of treatment and quality of life outcomes, but studies so far have been subject to methodological difficulties. Randomised controlled trials of screening for prostate cancer are underway in Europe, Canada and the US, but results in terms of differences in death rates are not expected to be available until about 2008 (Schroder et al. 1999).

Who has been tested?

There is widespread community concern about prostate cancer, reflected in the high rates of PSA testing in general practice. In a South Australian study, 20% of men age forty and over reported having a PSA test in the preceding twelve months (Pinnock, Weller & Marshall 1998), while in a NSW study, 22% men over fifty-five years had undergone testing in the same period (Ward et al. 1997). A national study reported that 27% of Australian men fifty years and over had had at least one test in 1995–96 (Smith & Armstrong 1998).

Few men who have PSA testing understand the next step if the result is abnormal (Pinnock, Weller & Marshall 1998), suggesting that they do not receive, understand or recall basic information about the test. A study in Western Australia reported that among men interviewed

who had undergone a PSA test, 80% recalled receiving fewer than five minutes education prior to the test (Slevin et al. 1999).

A review of Medicare-reimbursed PSA and prostate acid phosphatase tests from 1989 to 1996 found that an average of 300,000 tests were done in Australia each year over this period (Smith & Armstrong 1998).

Surveys in a number of Australian states have indicated a predominant role of the GP in initiating tests for prostate cancer, with up to 40% of GPs reporting a belief in the efficacy of PSA testing (Ward, Young & Sladden 1998; Pinnock, Weller & Marshall 1998). Other reasons identified for PSA testing were the presence of urinary symptoms, a family history of prostate cancer, a previously elevated PSA test, and concern expressed by the patient (Slevin et al. 1999; Ward, Gupta & Taylor 1998).

The policy context

Population screening for prostate cancer has been widely debated, with conflicting views being expressed. The Cancer Council supports the views of the expert reviews (AHTAC 1996; Weller et al. 1998; Harris & Lohr 2002) that current evidence does not support population screening of well men for prostate cancer.

Among the recommendations of the Australian Health Technology Advisory Committee (AHTAC) report (1996) were:

- that men being offered or requesting the PSA test be fully informed of the limitations of the available tests and the possible further diagnostic and treatment choices they may face if they have the test
- that research into prostate cancer continues to be targeted as a high priority funding area by the National Health and Medical Research Council (NHMRC) and other funding bodies
- that a mechanism be established to ensure that new technologies for screening, diagnosis and treatment of prostate cancer are rigorously trialled before being introduced into routine clinical practice, or, alternatively, that they are introduced under trial conditions involving appropriate professional bodies
- that a monitoring mechanism be put in place to ensure that the AHTAC position on screening is reviewed when significant developments occur
- that a comprehensive education program on the risks and benefits of prostate cancer testing be introduced for GPs, their patients and the community.

The Cancer Council and state and territory cancer councils were active in the establishment in 1998 of the National Prostate Cancer Collaboration to foster clinical, laboratory and epidemiological research, as well as research and programs in education. In 1999 the group became the Australian Prostate Cancer Collaboration (APCC). Its aim is to develop strategies for the prevention of prostate cancer to decrease mortality and increase quality of life.

Rationale for screening for prostate cancer

As discussed in the introduction to Section Two, the basis of the World Health Organization criteria for assessing screening is that there should be evidence that screening for the disease, with subsequent early intervention, is effective in improving health outcomes. In relation to prostate cancer, the issue is whether detection of tumours using currently available tests will result in benefits for patients.

The difficulty regarding early detection of prostate cancer is that first, depending on the age of the patient, many cancers found through screening will not be life threatening. Second, it is currently not possible to distinguish with certainty, those that will be life threatening. It has been estimated that prostate cancer is present in 30–40% of men aged more than fifty years, but only one in four of these cancers will result in clinical symptoms and one in fourteen will cause death (Weller et al. 1998).

The major treatment options following detection of prostate cancer are active treatment (surgical removal of the prostate or radiation therapy) or observational treatment (watchful waiting) (AHTAC 1996). Randomised controlled trials comparing options are difficult to conduct, but a recent study compared watchful waiting with immediate radical prostatectomy in 695 men with newly diagnosed early stage prostate cancer. Prostatectomy led to a significant reduction in both metastatic disease and disease-specific mortality, but not overall mortality (Holmberg et al. 2002).

In practice there is a wide variation in treatment decisions. Treatments for early prostate cancer differ in the proportion of patients who are likely to experience these side effects:

- erectile problems
- incontinence
- bowel symptoms.

However it has not been possible to prove definitively that they differ in effectiveness (NHMRC 2003). Consequently the incorporation of patient preference into treatment decisions is widely endorsed (Weller et al. 1998; NHMRC 2003).

Researchers such as Weller et al. have identified a number of problems in studies comparing the effectiveness of treatments:

- most information on treatment by surgical removal of the prostate comes from uncontrolled case series and cohort studies that indicate survival following surgery is high. However because surgical patients are usually younger and with less advanced disease, it is difficult to separate out the effects of treatment efficacy and selection bias
- a randomised controlled trial of 'watchful waiting' or 'no active treatment' compared with radical prostatectomy yielded fewer distant metastases and fewer deaths from prostate cancer in the surgery patients, but no statistically significant survival benefit from all causes (see Holmberg et al. 2002)
- radiation therapy is widely practised in Australia, particularly among older patients and those with more aggressive or later stage (high risk) cancers. Newer forms of radiation therapy aimed at increasing the radiation dose while minimising effects on adjacent tissues are becoming increasingly available.

Current clinical practice supports active intervention, particularly among men with aggressive and early onset of disease whose life expectancy exceeds ten years.

Would screening be of benefit at this stage?

The current state of knowledge does not satisfy the World Health Organization criterion that there should be an accepted treatment for patients with recognised disease. It is possible that intervention through early detection will cause more harm than good, for example in the risks posed by treatment (see below).

The problem of over-diagnosis

A major concern with screening is that it will diagnose cancers which, if left undetected, would never have caused morbidity or mortality. This is known as over-diagnosis. One estimate using mathematical modelling puts the over-diagnosis rate as high as 50% (Draisma et al. 2003). It has been estimated that most prostate cancer cases detected by commonly promoted testing strategies would not have caused morbidity or mortality (McGregor et al. 1998; Draisma et al. 2003). Over-diagnosis results in unnecessary treatment with high risks of urinary incontinence, bowel problems (especially following radiation) and erectile dysfunction (Begg et al. 2002).

Emerging issues

Prostate cancer testing in general practice

Recent reports suggest that GPs are poorly resourced to assist their patients making an informed choice on prostate cancer testing. Only half or less of the GPs who responded to a survey were aware of guidelines published by the Royal Australasian College of General Practitioners and The Cancer Council—both of which recommend against population screening (Ward, Young & Sladden 1998).

A meeting about informed choice for prostate cancer testing in general practice (Pinnock 2004) showed that:

- studies on how patients make medical decisions indicate that non-systematic factors such as old beliefs, anecdotes and salient experiences are more common than a systematic weighing up of pros and cons (see also Farrell, Murphy & Schneider 2002; Steginga et al. 2002)
- testing is often requested for medico-legal reasons. The process and content of an informed choice discussion needs to reflect medico-legal obligations
- criteria have been developed to assess which decision aids are likely to be most effective in helping patients become informed and make decisions
- the barriers GPs face in fully informing patients with diverse backgrounds and knowledge need to be better understood
- particular skills are needed in order to communicate complex issues such as uncertainty and risk to patients
- complicating factors are men's lack of access to primary care services, particularly in rural areas; poor general knowledge of male health in the community; and high prevalence and anxiety about urinary symptoms.

Cancer of the prostate is a common and important health problem. Its early diagnosis and subsequent treatment present a dilemma for medical practitioners and consumers. The tests and treatments for prostate cancer are examples of health interventions whose benefits and risks are not fully understood or appreciated either in the health community or in the Australian community at large. Individual men who decide to be tested for prostate cancer should be able to do so on the basis of informed consent, having access to full information about the potential benefits and risks associated with testing.

Aims

The Cancer Council supports:

- advocating for and contributing expert advice to the development of decision-making tools for informed choice about prostate testing, for medical practitioners and consumers
- contributing to the development and implementation of community education relating to the prostate and prostate cancer
- monitoring research on population screening for prostate cancer to inform the development of communication strategies
- seeking opportunities to work with health related agencies , health professionals and consumers to increase understanding of the prostate and prostate cancer.

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