EFFECTIVENESS Matters

SCREENING FOR PROSTATE CANCER

- There is increasing pressure on doctors to test men for the early detection of prostate cancer.
- Unlike breast cancer screening, which has been shown to reduce mortality, prostate cancer screening has not yet been evaluated and there are several reasons why it may be less effective.
- Many men with prostate cancer never experience any ill effects because some tumours are slow growing and not aggressive.
- The most sensitive screening tests for prostate cancer are based on levels of prostate specific antigen (PSA). However, the PSA test and follow up biopsies cannot predict reliably whether a man has a cancer that will progress to cause ill health or death.
- There have been no reliable evaluations of the effect of treatments for early prostate cancer on mortality. Active treatments can result in major complications such as incontinence and impotence.
- There is no evidence on the number of deaths (if any) which could be averted by screening asymptomatic men. Screening may lead to physical and psychological harm resulting from testing, biopsy and treatment. It is not known whether screening for prostate cancer does more good than harm.

Vol 2, Issue 2, February 1997

Effectiveness Matters is an update on the effectiveness of health interventions for practitioners and decision makers in the NHS. It is produced by researchers at the NHS Centre for Reviews and Dissemination at the University of York, based on high quality systematic reviews of the research evidence. ***Effectiveness Matters*** is extensively peer reviewed by subject area experts and practitioners.

The NHS Centre for Reviews and Dissemination is funded by the NHS Executive and the Health Departments of Scotland, Wales and Northern Ireland; a contribution to the Centre is also made by the University of York. The views expressed in this publication are those of the authors and not necessarily those of the NHS Executive or the Health Departments of Scotland, Wales or Northern Ireland.

THE UNIVERSITY of York

NHS CENTRE FOR REVIEWS AND DISSEMINATION

There is interest in the early detection (screening) of prostate cancer because treatment of advanced disease is relatively ineffective. Public awareness of benign and malignant disease is increasing. However, the appropriateness of testing for early stage prostate cancer is uncertain.

This bulletin summarises research evidence about the effectiveness of prostate cancer screening. It is based upon the findings of recent systematic reviews carried out in several countries.[1-12]

PROSTATE CANCER - BACKGROUND

Prostate cancer is the third commonest cancer death in men after lung and large bowel with a mortality rate of about 34 per 100,000 males. The incidence of prostate cancer increases with age; only 12% of clinically apparent cases arise before the age of 65. People with a family history of prostate cancer are at higher risk of the disease. Men presenting with lower urinary tract symptoms are not at increased risk of prostate cancer.

The rate of registration of prostate cancer has been steadily rising. This is probably due to the ageing of the population, increased diagnostic accuracy and recording of cases, and increased detection due to more frequent surgery for BPH. Most of the 40% rise in incidence reported in the USA is due to more cases being picked up by widespread prostate cancer screening,[13] a practice which is not common in the UK.

There is considerable uncertainty about the natural history of prostate cancer. Autopsy studies show that 30% of men over 50, who had no symptoms of prostate cancer whilst alive, have histological evidence of prostate cancer at the time of death. This percentage rises to over 50% in men over 80 years of age.[7] In other words, most men with prostate cancer die with, rather than from, the disease. This is because most prostate cancers in the population are slow growing and unlikely to cause clinically important symptoms during a man's life. Obviously, prostate cancer in younger men has a greater chance of clinically progressing because of their longer remaining life span. A minority of cases of prostate cancer do progress rapidly, invading the surrounding tissues and metastasising, usually to the bone.

EVALUATING SCREENING

The aim of screening is to identify, at an early stage, those cases of prostate cancer which will become invasive and then to offer treatment which will increase the quality and length of life. Although it seems common-sense that early detection of a cancer will be beneficial, this has not always proved to be the case. Screening needs to be rigorously evaluated to assess whether it does more good than harm.[14] The effectiveness of a screening programme can best be determined by means of randomised controlled trials (RCTs).

Several RCTs showed that breast cancer screening can reduce mortality. However, despite the widely held belief that lung cancer screening was effective, RCTs evaluating early detection of cancer of the bronchus found no effect on mortality and even some harm, due to unnecessary surgery.[15]

No rigorous evaluations of prostate cancer screening have been carried out, so the overall effects are unknown. The current enthusiasm for prostate cancer screening in the USA has been compared with the premature advocacy of lung cancer screening 30 years ago.[15]

Before screening tests are used, doctors must be convinced that there are benefits for patients and that these outweigh the potential harms of investigating healthy people with no cancer, the anxiety associated with having a test and the complications of treatment. Also to be considered are the effects of intervening in apparently healthy people, who, although found to have prostate cancer, would never suffer any adverse consequences from the disease.

A provisional assessment can be made by examining the accuracy of the screening test and the effectiveness of treating prostate cancer at an early stage (see box).

Benefits and harms of prostate screening will depend on:

- how well the test distinguishes people who do from these who do not have early stage prostate cancer.
- the extent to which those cancers which are likely to cause clinical problems can be distinguished from the majority of tumours which will not present clinically.
- the adverse physical and psychological effects of the screening tests and the further investigation of those with raised PSA levels.
- the beneficial and harmful effects of treatment on the quality and length of life.

THE EVIDENCE

Accuracy of the Test

There are three recognised methods of screening for prostate cancer: digital rectal examination (DRE), transrectal ultrasound (TRUS) and measurement of levels of serum prostate specific antigen (PSA). Sometimes combinations of these tests are used. Comparisons of screening tests carried out on the same asymptomatic patients

show that a raised PSA level above 4ng/ml is a more sensitive test than DRE or TRUS.

PSA is a glycoprotein produced specifically by the prostate gland but not specifically by prostate cancer. The presence of BPH and prostatitis can also raise PSA levels and produce false positive results. Only around a quarter to a third of asymptomatic men with abnormally high PSA levels will subsequently be shown to have prostate cancer.

The accuracy of the PSA test may be improved by using age specific cut-off values, the ratio of free to bound PSA, ratio of PSA serum concentration to gland volume, and rates of change in levels over time. None of these has yet been sufficiently well evaluated to determine which is the best one.

Effects of Testing and Further Investigation

An abnormal PSA test result is frequently followed by a repeat PSA measurement because of high test-retest variation (up to 30%). If the second test is also elevated, transrectal needle biopsy (TRNB) of several segments of the prostate is carried out under ultrasound guidance. The results of the biopsy can help predict the likelihood of tumour progression. Approximately two thirds to three quarters of all those investigated will not have prostate cancer. TRNB can be uncomfortable, can result in infection in up to 5% of patients and, rarely, major bleeding. There is no reliable evidence that needle biopsy assists the spread of cancer cells.

Detecting Clinically Important Tumours

Screening for prostate cancer only has the potential to reduce mortality if it can distinguish those clinically important cancers which behave aggressively from those of little clinical significance. Studies of the size and differentiation of tumours detected by PSA screening, and of the proportion which already show signs of extension beyond the capsule[8] or metastases, suggest that about a third of cancers detected through PSA screening show signs of being aggressive and clinically important.

Whilst poor differentiation and other unfavourable histopathological characteristics are associated with decreased survival from prostate cancer, neither these findings nor PSA results can reliably predict whether a cancer is likely to progress to ill health or death.

Effectiveness of Treatment

Detecting prostate cancer early will be of little value if patients cannot then be offered effective treatment. The main options for treating clinically localised prostate cancer are watchful waiting, radiotherapy and radical prostatectomy.

Recommendations

- **Routine testing of men to detect prostate cancer should be discouraged, irrespective of family history.**
- **Purchasers should not fund screening services for prostate cancer.**
- **Evidence from randomised controlled trials of prostate cancer screening using PSA (or similar tests) and treatment are needed before consideration is given to funding prostate screening.**
- **Patients enquiring about prostate screening should be clearly informed about the current state of evidence on the benefits and harms of screening and treatment.**

Watchful Waiting is the most common policy in the UK. This varies from waiting until the patient presents with symptoms to more active follow up of outpatients with regular PSA testing and physical examination. Although this strategy does not produce the physical or sexual complications associated with other treatments, it may increase anxiety.

Radiotherapy uses an external beam of x-irradiation aimed at the prostate. Complications include damage to adjacent organs such as the gastro-intestinal tract and bladder (36% of patients) incontinence (around 1-6%) and impotence (40%).

Radical (total) prostatectomy entails removing the entire prostate. Complications include operative mortality (up to 1%), complete incontinence (1-27%) and impotence (20-85%). However, some patients are willing to trade off more morbidity for assumed increased survival.[16] Radical prostatectomy is rarely, but increasingly, carried out for localised disease in the UK but is a common first line treatment in the USA.

There is uncertainty about the effects of these treatment strategies because no RCTs have reliably evaluated them.[3] The currently available research indicates that survival with any of these options is relatively high and does not suggest a significant difference in mortality between the three treatments.

OVERALL BENEFIT AND HARM

The benefits of screening are uncertain. There is no reliable evidence to determine whether or not early detection and treatment of prostate cancer

improves survival. Annual testing with PSA will detect a number of clinically important cancers, but it is also likely to over-detect those cancers which are not clinically important. There is no direct evidence to show that men with well and moderately differentiated disease benefit from active treatment. The possible harmful effects of screening and treatment which needs to be considered alongside the uncertain benefits may include: increased anxiety, the discomfort of biopsies and the risks of incontinence, impotence, radiation damage to the rectum and bladder and, possibly, death if more aggressive treatments are adopted.

Decision models attempting to estimate the net effect of screening suggest that the harmful effects on quality of life are likely to outweigh the benefits especially if radical prostatectomy is the first line treatment.[4-6] One model predicts that prostate cancer screening produces a net loss of quality-adjusted life expectancy of 3 to 13 days.[4] However, these conclusions are dependent on the assumptions used.

It is only ethical to offer someone a screening test when it is likely to do more good than harm. Given the lack of evidence of benefit and the possibility of harm, prostate screening tests do not appear to be justified outside of a rigorous evaluation.

Patients who inquire about a test assuming that screening is effective should receive clear information on the likely benefits and harms of testing, investigation and treatment and their implications. Giving such information has been shown to influence patient choices.[17] A patient information sheet has been produced to accompany this bulletin.

Doctors may also feel pressured to carry out PSA testing due to the fear of not detecting prostate cancer. However, there is no reliable evidence that detecting it benefits patients. People with a family history of prostate cancer may be particularly concerned about their increased risk of developing the disease but, regardless of one's risk, there is no direct evidence that treatment is beneficial.

REFERENCES

1 Green CJ, Hadom D, Bassett K, Kazanjian A. ***Prostate specific antigen in the early detection of prostate cancer.*** Vancouver:B.C. Office of Health Technology Assessment, 1993.

2 Kramer BS, Brown ML, Prorok PC, Potosky AL, Gohagan JK. Prostate cancer screening: what we know and what we need to know. ***Ann Intern Med*** 1993;119:914-923.

3 Wasson JH, Cushman CC, Bruskewitz RC, Littenberg B, Mulley AG, Wennberg JE et al. A structured literature review of treatment for localized prostate cancer. ***Arch Fam Med*** 1993;2:487-493.

4 Krahn MD, Mahoney JE, Eckman MH, Trachtenberg J, Pauker S, Detsky AS. Screening for prostate cancer: a decision analytic view. ***JAMA*** 1994;272:773-780.

5 Hanley JA, McGregor M. ***Screening for cancer of the prostate: an evaluation of benefits, unwanted health effects and costs*** Conseil d'evaluation des technologies de la sante du Quebec, Montreal, 1995.

6 US Congress, Office of Technology Assessment. ***Costs and effectiveness of prostate cancer in elderly men*** OTA-BP-H-145. Washington, DC:U.S. Government Printing Office, 1995.

7 Woolf SH. Screening for prostate cancer with prostate specific antigen: an examination of the evidence. ***New England Journal of Medicine*** 1995;333:1401-1405.

8 Australian Health Technology Advisory Committee. ***Prostate cancer screening*** Canberra:AHTAC, 1996.

9 Chamberlain J, Melia J, Moss S, Brown J. ***T***he diagnosis, management, treatment and costs of prostate cancer in England and Wales. ***Health Technology Assessment*** 1997;1(3).

10 Selley S, Donovan J, Faulkner A, Coast J, Gillat D. Diagnosis, management and screening of early localised prostate cancer: a systematic review. ***Health Technology Assessment*** 1997;1(2).

11 US Preventive Services Task Force. ***Guide to clinical preventive services***, 2nd ed. Baltimore:Williams & Wilkins, 1996, ch 10.

12 SBU Mass screening for prostate cancer. ***Int J Cancer*** 1996; 9 (Suppl): 1-72.

13 Potosky AL, Miller AB, Albertsen PC, Kramer BS. The role of increasing detection in the rising incidence of prostate cancer. ***JAMA*** 1995;273:548-552.

14 Wilson JMG, Jungner G. ***Principles and practice of screening for disease*** Geneva:WHO (Public Health Paper), 1968.

15 Collins MM, Barry MJ. Controversies in prostate screening: analogies to the early lung cancer screening debate. ***JAMA*** 1996;276:1976-1979.

16 Jonlar M, Messing EM, Rhodes PR, Bruskewitz RC. Sequelae of radical prostatectomy. ***Br J Urol*** 1994;74:352-8.

17 Wolf AMD, Nasser JF, Wolf AM, Schorling JB. The impact of informed consent on patient interest in prostate-specific antigen screening. ***Arch Intern Med*** 1996;156:1333-1336

FURTHER INFORMATION

If you would like further information please contact:
General Enquiries: 01904 433634
Information Service
(including databases): 01904 433707
Publications: 01904 433648
Fax: 01904 433661
Email:revdis@york.ac.uk
University of York, Heslington, York, YO1 5DD.

THE UNIVERSITY of York

NHS CENTRE FOR REVIEWS AND DISSEMINATION

Promoting the application of research-based knowledge in health care.