

Decision making

Prostate disease: management options for the primary healthcare team

Report of a working party of the British Prostate Group

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Summary

The prostate gland has attracted a remarkable increase in interest in the past few years. The two most common diseases of this gland, benign prostatic hyperplasia and carcinoma of the prostate, have been brought into greater prominence by new diagnostic methods, public interest, and a wider choice of surgical and non-surgical treatments. Uncertainty about the significance of these changes has occurred because of the rapidity of change, the profusion of statements, opinions and promotions, and the relatively little guidance available from the profession.

Ten urologists and two general practitioners have reviewed the relevant evidence about these two prostate diseases and the newer diagnostic methods; their conclusions are summarised here. Management options and guidance on clinical practice are also discussed. Because of a number of unresolved diagnostic and management issues, detailed requirements for practice guidelines have not been specified.

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Introduction

The two most common diseases of the prostate gland, benign prostatic hyperplasia (BPH) and carcinoma of the prostate, have attracted a remarkable increase in interest in the past few years. Of those with symptoms of BPH, about a third will have surgical treatment and the remainder may either improve or do not worsen; this variation in the natural history must be considered when evaluating any new method of treatment.¹

It has been estimated that the probability of a 40-year-old man undergoing a prostatectomy in his lifetime is 29%.² More than 90% of men who have a prostatectomy will have a transurethral resection of the prostate and approximately 40 000 resections are carried out in the UK each year. This operation has come under scrutiny recently because of the claim that it may not have such a good outcome as most urologists believe,^{3–5} there also appears to be a higher incidence of late mortality following a transurethral resection compared with an open prostatectomy.⁶ In parallel with these reports there has been a dramatic increase in the number of new procedures and new products, each claiming efficacy in the treatment of BPH with only minimal side-effects and no mortality.^{7–10}

Cancer of the prostate is also a very common disease, ranking the fifth most common cancer in the world. In some advanced countries it has become the most common cancer in men, due mainly to improvement in methods of diagnosis (see box). Incidence and mortality rates vary widely due in part to the varying quality of data collected and also to a striking difference in incidence in different parts of the world. There may also be an absolute increase in cancer of the prostate. The age-adjusted incidence rate for cancer of the prostate in US blacks is nearly twice that of US whites, which in turn is twice the reported rate in the UK (ie, 20/100 000) age adjusted. Age-adjusted mortality rates in the US and in the UK are very similar.^{11,12} The major difficulty in understanding the different attitudes to diagnosis and treatment of cancer of the prostate lies in these large differences in incidence and mortality and also in the high proportion of prostate cancer found coincidentally and which only infrequently is the cause of death; these have been called latent or clinically insignificant cancers – expressions which appear to be at variance with the generally accepted concepts of cancer biology.¹³ Thus, improved methods of diagnosis will certainly detect many more of these small tumours but whether they will need treatment or cause death is highly debatable.

Diagnostic methods have developed rapidly and these have influenced the current attitude to both benign and malignant disease. The traditional digital rectal examination can now be supplemented by transrectal ultrasound of the prostate which both measures prostate volume and localises morphological abnormalities.^{14,15} Ultrasound can also be used to measure residual urine, thereby avoiding catheterisation.

A development of even greater impact has been the increasing use of the blood test for prostate-specific antigen (PSA) which is not a specific marker for cancer of the prostate but is better than prostatic acid phosphatase, a test now abandoned by most laboratories.^{16–18} The increasing use of the PSA test has led to many problems of interpretation and the Working Party sought to clarify these issues.

What is the place for prostate screening?

The word screening is often misused. The popular use of the word is in the context of population screening, which includes persons who are asymptomatic.

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Benign prostatic hyperplasia

- 80% of men over 60 years
- 25% seek medical advice
- 33% undergo surgical treatment

Cancer of the prostate

- 12 000 new cases annually (UK)
- present in 70% of men over 80 years
- only clinically manifest in 0.4% cases

Remit of working party

- What is the place for prostate screening?
- What is an optimum urological history?
- What is the role of the digital rectal examination?
- What is the role of PSA?
- When to seek a specialist opinion
- GP monitoring of patients with BPH
- GP monitoring of patients with prostate cancer

The recommended terms are mass screening for large-scale screening of whole populations, selective screening for certain high-risk groups in the population and case-finding for the screening of patients already in contact with a primary health-care service.¹⁹

These distinctions are important because it is case-finding that most doctors mean in respect of prostate disease: much debate centres on whether to proceed further to mass screening.

There is evidence that a substantial proportion of men with micturition symptoms and/or poor urinary flow rates do not consult their GPs (primary health-care physicians),²⁰ the widely stated reason for not seeking advice is 'I know it is just my age'. With better education in medical matters this stoicism is changing.

Despite several pilot studies to assess the place of screening for prostate disease,²¹ there is at present no support for mass screening because there is no evidence of benefit, something that will require large-scale trials to establish.²²⁻²⁴ Once there is a consensus on the benefits of early intervention, a case could, however, be made for selective screening of men who are in one of the risk groups (see box on next page).

In practice, more GPs will case-find, ie, screen patients who consult them because (a) they have symptoms of micturition difficulty (they may also consult because of other medical problems but then reveal micturition difficulties), or (b) though asymptomatic, they are seeking advice or wanting to be checked.

THE ASYMPTOMATIC MAN

The attitude of the medical profession in the UK to asymptomatic men has not yet been defined. The practice of regular health check-ups has only been adopted by a small proportion of the population and is not generally encouraged. However, publicity and pressure through articles in popular magazines²⁵ and through the media about prostate problems is increasing. Compared with the number of well-woman clinics, there are relatively few well-man clinics although some GPs are now offering this service as part of their 'Health Promotion' package.

If a man over 50 years old seeks advice about his prostate (see box), he should be advised that the findings on digital rectal examination and PSA may require further tests to determine their significance.²⁶ A prostate assessment in men under the age of 50 is not recommended because the detection rate of abnormalities is extremely low.

THE SYMPTOMATIC MAN

The situation for a man over 50 years of age with some micturition symptoms is not so different except that GPs will need to consider whether they might either institute treatment or refer for a urological opinion. Until recent times, a man with mild to moderate symptoms would have had these explained to him and probably not been offered treatment or specialist referral. Now that there are several non-operative choices, GPs may want to consider prescribing medications. However, the same minimal recommendations are made: (1) examination, (2) digital rectal examination and (3) PSA, before making a decision. The PSA test is mandatory if medical treatment is to be prescribed. Some GPs may feel happy to carry out this minimal screen and, if negative, prescribe treatment; others may not be willing to prescribe before confirmation of their findings by a urologist.

What is an optimum urological history?

An optimum history should focus on the following:

Are the symptoms due to the prostate?

An alteration in urinary habits, just as an alteration in bowel habits, is a warning that there may be a pathological process to be identified. Irritative symptoms rather than obstructive symptoms should alert to the possibility of a range of pathologies – cancer of the bladder or rectum; diverticular disease; diabetes mellitus; or neurological abnormalities such as parkinsonism. Anxiety, depression, and alcoholism are common and may also affect micturition. A past history of sexually transmitted disease may be relevant as a cause of urethral stricture.

Some urologists are trying to quantify symptoms by the use of a questionnaire or symptom score but none of the score systems can yet be recommended for general use.²⁷ Similarly, frequency and/or volume charts kept by the patient are widely used to evaluate women with micturition problems and their use is increasing for men; however, in men, these charts only give a guide to the problem and their use has not yet been validated.

**Prostatic cancer:
risk groups**

- over 50 years of age with a family history of carcinoma of the prostate (those whose father or brother had prostate cancer are twice as likely to have the disease)
- over 50 years of age in black races (especially in the US where the age-adjusted incidence for blacks is 3–4 times greater than for a white man in the UK)

Prostatic cancer: screening

- physical examination to include external genitalia and abdomen
- digital rectal examination
- prostate-specific antigen test, after discussion on the implications of the test with the patient

PSA test

- normal range 0–4.0 ng/ml
- > 4.0 ng/ml: BPH, prostatic cancer, prostatitis, prostatic infarction
- > 10.0 ng/ml: 2/3 will have cancer
- > 60.0 ng/ml: all will have metastatic cancer

Between 25% and 30% of patients with micturition symptoms attributed to the prostate have no evidence of obstruction on pressure-flow studies.²⁸ If a GP wishes to treat symptoms it is not essential to demonstrate that the patient has outflow obstruction. However, the measurement of a urinary flow rate is a very helpful adjunct in the assessment though it will not necessarily identify all forms of voiding dysfunction in men.

Is the prostate malignant?

There are no specific symptoms that answer this question. Digital rectal examination and a PSA test are essential preliminaries in the resolution of this doubt. Only a few patients will present initially with symptoms of secondary deposits.

Has the patient physical signs of urinary retention or is he liable to develop retention?

An abdominal examination should resolve part of this question and an abdominal ultrasound, if available, will help to determine if there is a measurable residual urine. Predicting the likelihood of acute retention is almost impossible: in a longitudinal study only three of 100 patients with micturition symptoms followed for five years, developed acute retention.²⁹

Is the management of this patient within my expertise?

Some GPs will be satisfied that they have the knowledge and experience to answer the questions; others may prefer to refer to a urologist.

The role of the digital rectal examination

The place of a rectal examination, especially in the assessment of a male with micturition symptoms, remains important. The information gained from examination of the prostate may not be highly specific either for benign enlargement or for malignant disease but it does exclude abnormalities of the anus and lower rectum and it does help the doctor judge the urgency of the prostate problem.

A digital rectal examination provides a guide to the size of the gland and, although it will not pick up early focal lesions, can help to detect some malignant lesions. A screening detection rate for prostate cancer of 1.7% has been found using rectal examination alone.³⁰ This compares with an overall detection rate of 2.4% achieved by the American Cancer Society National Prostate Cancer Detection project, with the addition of PSA and transrectal ultrasound.³¹

A study using a combination of digital rectal examination, PSA, and ultrasound in a population of men who were symptomatic or had been referred to a urology clinic with suspected prostate cancer resulted in a detection rate of 14.6%. Out of the 263 patients found to have carcinoma in this study, 123 patients had palpably suspicious areas. Thus, although an annual rectal examination is no protection in terms of risk of developing prostate cancer, it is important that this test should now be considered, together with a PSA test (see later), to increase the detection rate.¹⁵

In addition, even though most GPs may do a digital rectal examination only a few times each month, this, coupled with the examination of the genitalia and abdomen, will help to detect associated pathology and may also act as a guide to the degree of urgency when a referral to a specialist is initiated.³⁰

What is the role of prostate-specific antigen?

PSA is produced exclusively by epithelial cells of the prostate gland and therefore is a measure of the activity of these cells. It is not specific for either cancer or benign hyperplasia.³² Interpretation of a PSA test result is not straightforward because the values may vary according to the test used and there is debate about the definition of normal values (see later).

In Britain, the most commonly used test (Hybritech) has a normal range of 0–4.0 ng/ml. An upper limit of normal of 4.0 ng/ml is commonly used but it does not preclude a patient from having a localised cancer.^{15,17} For practical purposes a patient with PSA values less than 4.0 ng/ml and a normal rectal examination does not require further assessment. Recently, age-specific reference ranges have been recommended; these are probably a reflection of prostate volume which is also directly related to age (table 1).^{33,34} A normal value does not exclude the subsequent development of a prostate cancer. Studies show that between 5% and 10% may have normal values yet also have a non-palpable focal lesion – the so-called latent or clinically insignificant tumour. The American Cancer Society project referred to earlier, found that 40% of the men who were diagnosed as having prostate cancer had normal PSA values, so it is possible that the

Table 1 Age-specific reference ranges for PSA values³⁴

Age range (years)	PSA (ng/ml)
40–49	3.0
50–59	4.1
60–69	5.6
70–79	7.6

Table 2 Risk of prostate cancer related to PSA values (adapted from Cooner¹⁹ and Catalona²¹)

PSA (ng/ml)	Risk of prostate cancer (%)
<4.0	4–11
4–10	17–26
>10	50–64

proportion of men with occult lesions and normal PSA values is even higher than 10%.³¹

The more difficult values to interpret are 4–10 ng/ml where the risk of having prostate cancer is 17–26% (table 2). Values in this range are therefore more commonly due to BPH alone and a correction factor for volume has been recommended.³⁵ However, it has also been recommended that multiple biopsies of the prostate should be done because of the risk of cancer. The age and general condition of the patient are clearly of major importance in deciding the best course of action.

It might be argued that a PSA test is a good way of finding early and presumably curable prostate cancer. Unfortunately the biology of this tumour is not always predictable: whilst stage and grade are essential prognostic factors, the prevalence of early stage, small volume cancers is common. There are approximately six million men in the UK aged between 50–75 years and it is likely that up to 40% (more than two million) have a focus of cancer, yet the clinical incidence in that population is only 12 000 and the death rate for cancer of the prostate is about 3%. At present the mean age of presentation in the UK is 72 years.

Undoubtedly the use of PSA values and the increased use of multiple biopsies will find more of these cancers¹⁵ and thereby lower the age of presentation but many will have an almost zero malignant potential and will never need treatment. There is no clear answer as to what is the best advice to give. The debate continues and will not be resolved until there have been clinical trials comparing conservative (ie, no immediate treatment) with radical (ie, surgery or radiotherapy) treatments.

This summary of the dilemmas posed by the ready availability of PSA tests must be considered by all who order this test to evaluate/screen their patient. Both physician and patient can gain reassurance from a normal value but the finding of even a mildly raised value leads to a commitment to further assessment.²⁶ Also the finding of a normal value is no protection against the presence or subsequent development of prostate cancer.

In order to avoid immediate biopsy for a mildly elevated value, a repeat value at say 6–12 months is the preferred option for those patients who, because of age and general condition, would not be candidates for radical prostatectomy. There are no firm data on which to support any particular time interval but studies of the rate of rise of PSA suggest it might be possible to make a prediction of cancer in some men. A steady state requires no action but a rising value needs closer observation and may lead to biopsy.³⁶

When to seek a specialist opinion

The decision to refer a man with urinary symptoms is more likely to be based on subjective than on objective findings. The absolute indications are acute retention, a clinically palpable bladder or distended bladder detected by ultrasound, either gross or microscopic (stix) haematuria, or a suspiciously hard prostate. Pain or discomfort on micturition, including bladder pain, can be associated with bladder cancer and therefore needs further assessment. The role of a PSA test has been discussed but the role of a serum creatinine in deciding about referral is less precise. The man with mild to moderate symptoms and a normal physical examination, except for some enlargement of the prostate, will be judged mainly on the basis of the level of quality of life disturbance these cause him, the competence of the GP in the assessment of the symptoms, the overall quality of life and the general medical state of the patient (see flow chart). The varying prostatectomy rates in different countries and different parts of a country emphasise the subjective nature of these assessments. The World Health Organisation³⁷ and American Urological Association³⁸ have published diagnostic guidelines and the American Agency for Health Care Policy and Research³⁹ has followed with clinical guidelines on BPH. The relevance and application of these guidelines has to take into consideration the healthcare infrastructure and resources available within the UK.

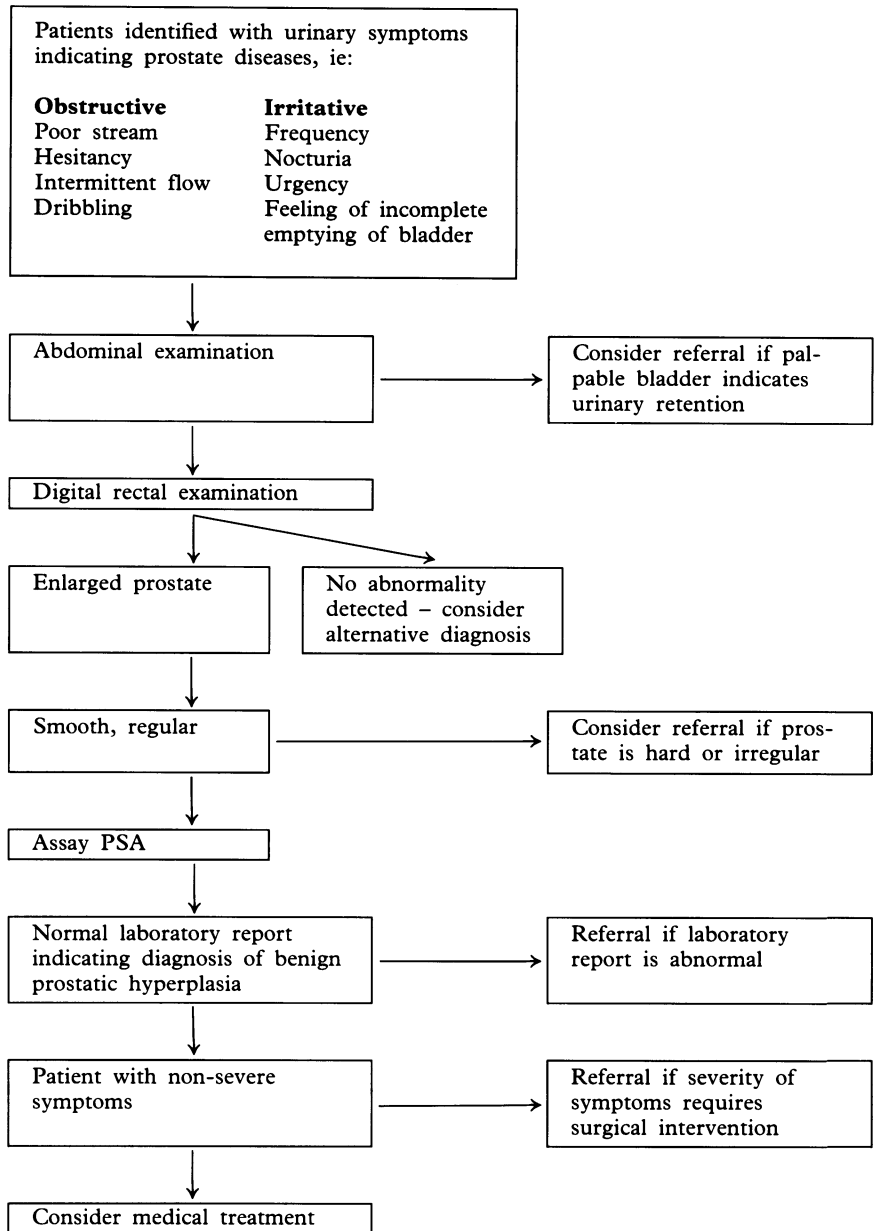
The decision by a GP to treat a patient with one of the medications recommended for BPH may be made either as a temporary way of alleviating symptoms pending specialist referral or as a specific treatment having excluded factors that might warrant a urological opinion. The patient who fails to respond to prostate medication within 3–6 months should be considered for referral.

Once the decision is made for a referral, the GP should try and judge the degree of urgency based on physical findings and possibly a PSA measurement.

Prostate Disease Flowchart

Primary Care Management

Referral to Urologist



GP monitoring of patients with BPH

PATIENTS IN WHOM SURGERY HAS NOT BEEN RECOMMENDED

Following discussions about the suitability of shared care, the urologist, having made his initial assessment of the prostate, may ask the GP to take over the follow-up, including the supervision of long-term BPH medication. In taking on this responsibility there are two specific concerns that need to be addressed. The first is the likelihood of acute retention: this is a wholly unpredictable event and only general advice about factors that can aggravate retention can be given to the patient. The second concern is the risk of developing cancer of the prostate. The high prevalence of malignant change in a prostate emphasises that there will be patients on BPH medication who ultimately develop a cancer. For this reason an annual rectal examination and PSA test is recommended for any man undergoing any form of non-surgical treatment for micturition symptoms.

PATIENTS WHO HAVE HAD A TRANSURETHRAL PROSTATECTOMY

The majority of urologists prefer to see their patients for at least one follow-up consultation after a transurethral prostatectomy, if only to assess the short-term outcome of the operation. Subsequent follow-up can be given by the urologist or the GP, the choice being negotiated locally.

The late outcome is of concern for two reasons. Firstly, consideration has to be given to possible cardiovascular complications.^{40,41} Secondly, there is the possibility of the development of further outflow symptoms, or their persistence in spite of surgery, and the possible need for medication or further surgery. Should the need arise, the choice between medical or further surgical treatment will usually be made by the urologist whether or not the long-term supervision of men on BPH medication is carried out by the patient's GP.

Monitoring of patients with prostate cancer in primary healthcare

The role of the GP, after primary treatment has been initiated, will vary according to the facilities offered by the urologist and by the particular interests of the GP. This relationship becomes of increasing importance if or when the patient either fails primary hormone control or develops progressive disease after radical treatment. When orchidectomy is chosen as primary hormone treatment, follow-up may be carried out by either the general practitioner or the urologist. When monthly luteinising hormone releasing hormone treatment has been chosen and is given by the GP, this also provides a close regular follow-up. Symptoms and signs should be monitored regularly (six monthly) and the PSA repeated at six-monthly intervals to assess progress. A bone scan will be needed – for which referral back to the urologist will almost certainly be necessary – if and when there are indications of possible bone deposits.

PSA is a valuable monitor of prostate cancer but two particular problems can arise: the first is that the patient may become focused on the PSA value to the point where both he and his family have an almost morbid interest in the value and any change in that value. The second problem is the interpretation of a rising PSA in the absence of any clinical or symptomatic change: whether or not any of the relatively ineffective second-line treatments should be given on the basis of the PSA change alone has not yet been established and will require controlled clinical trials. Prostate cancer is an exceptional cancer in that the urge to do something may not always be the best decision.

The main second-line treatment in prostate cancer is to control pain, mainly that associated with secondary deposits in the bone. However, the role of a bone scan is diminishing in the face of more experience with PSA. Routine follow-up bone scans are no longer necessary but when bone metastases are suspected then it is useful to quantify the extent of the disease by a bone scan.

Terminal (palliative) care

There are a number of strategies for pain control to be considered and this is best done by the shared responsibility of GP and urologist together, when appropriate, with a hospice physician. The aim of management in the later stages of cancer of the prostate is always to ensure an acceptable quality of life.

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