12 Benign Prostatic Hyperplasia

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1 Summary

Introduction and statement of problem

Symptoms of lower urinary tract dysfunction are very common in ageing men and women. They are found in 25 to 40% of men aged over 60 years and are not synonymous with benign prostatic enlargement (BPE), which is found in about 30% of men aged over 60. Histological evidence of benign prostatic hyperplasia (BPH) is found in more than 50% of men aged over 60.

Serious complications can occur as a consequence of BPE. Of men in England undergoing prostatectomy, no fewer than 25% presented with acute retention of urine, which carries a twofold risk of death and complications compared with prostatectomy for symptoms alone. Chronic urinary retention can lead to renal failure and is an indication for 15% of prostatectomies carried out in England and Wales. Other complications such as bladder stone, infection and haematuria can also occur. Nevertheless, the majority (*c.* 60%) of men undergoing prostatectomy do so electively because of the presence of symptoms.

However, men undergoing prostatectomy (42 000 per year in England and Wales) represent the minority of those presenting to the general practitioner with lower urinary tract symptoms (LUTS). LUTS are frequently caused by pathology other than BPE, including ageing-related changes in the bladder smooth muscle (detrusor muscle), idiopathic detrusor instability (phasic changes in bladder pressure found during filling, giving rise to symptoms of urgency and frequency) and prostate cancer. The GPs need to develop protocols for referral and assessment with the local urological team.

In the past, most men in the UK with LUTS were not actively treated by their GP. Men either did not complain or were managed conservatively. The advent of new drugs (mainly α-adrenergic blockers and 5-α-reductase inhibitors) is more likely to increase the total proportion of men treated in primary care rather than reduce the rate of operative treatment (because of the relatively low baseline rates of operative treatment in the UK, which is often performed for complicated BPE). Prescriptions for α-adrenergic blockers have increased from 812 400 per annum in 1995 to 1 207 300 per annum in 1997, whereas prescriptions for finasteride (a 5-α-reductase inhibitor) have been relatively constant (from 279 200 per annum in 1995 to 299 100 per annum in 1997).

Within hospitals, a number of new technologies have been introduced, mainly in efforts to decrease the need for inpatient beds. However, in most instances such new technology has not been compared in large randomised trials with conventional treatments. Many men treated with such capital expensive new technology may also subsequently need conventional treatment.

Patients needing operative treatment are usually classified under the following codes:

- ICD 10 general symptoms: N320a, N40a, N320b, R39, N40b
  retention: R33a, R33b, R33c, R33d, R33e R33f
  BPH: N40c, D291.
- Read codes: general symptoms: X30Nx, X30O0, K160, 1AA, X30Nz
  retention: 1A32, X30O4, X30O5, X30O6, X30O7, X30O8
  BPH: K20, B7C2.

Operative procedures on the prostate done for BPE include the following codes:

- OPCS4: M619, M612, M613, M641, M704, M678b, M678e, M678d, M652a, Y118, M672, M671, M662, M658a, M651b, M651a, M651c, M678a, M658b.
- Read codes: 7B360 (*Note*: this is radical prostatectomy, usually done for cancer), 7B361, 7B362, 7B372, 7B380, 7B3C4, X30FN, 7B3B5, 7B3B7, 7B3B8, 7B391, X30FP, 7B3B6 (qual), 7B360, 7B3A1, 7B393, 7B390, X30FK, Xa40r (qual), X30FM, X30FL.
- HRG codes: L29, L30, L31, L32.

Sub-categories of lower urinary tract symptoms (LUTS) and complications caused by benign prostatic enlargement (BPE)

Men presenting with LUTS can be classified according to the severity of symptoms and the degree of problems they experience (mild, moderate or severe). They can also be classified according to whether they have symptoms alone or complications which require more urgent treatment. The main subgroups are:

1 symptomatic categories based on severity and on degree of problems:
   - severe
   - moderate
   - mild
2 complicated BPE:
   - acute retention
   - chronic retention
   - chronic sepsis and bladder stones.

The prevalence of LUTS

Histological BPH is very common, being found histologically in more than 50% (500/1000) of men aged more than 60 years. Moderate to severe LUTS (roughly equivalent to those in men undergoing prostatectomy) are found in the community in 15 to 35% (*c.* 300/1000) of men aged more than 60 years. In general, many men in the UK have accepted such symptoms as being associated with ageing and have not consulted their GP. This is changing, however, because of publicity about men's health, worries about prostate cancer, and the advent of new drugs and new treatment methods (*see* Appendix 1), which are likely to increase the total proportion of men with symptoms who are treated.

Services and treatments available and cost

Costs are based on mid-1998 figures. Men with LUTS are assessed by their GP before referral to the urologist. Increasingly, assessment in primary care might include a more thorough assessment, which could involve measurement of urinary flow rates.

Non-operative treatment includes 'watchful waiting' or initial treatment with α-adrenergic blockers or finasteride.

Investigations in hospital include measurement of flow rates and, in some cases, bladder pressure tests (urodynamics) to determine whether symptoms are caused by prostatic enlargement. Such visits would cost a total of £250 to £300 (including tests and subsequent reattendance).

Increasingly, hospitals or GPs are setting up nurse-led prostate assessment clinics which can provide easy access to a full history, clinical examination, flow rates, prostate assessment and, subsequently, feedback to GPs. At first sight, these clinics would seem likely to be cost-effective, but they have not been fully assessed, nor have they been fully costed.

Conventional surgical treatment includes transurethral resection of the prostate (TURP), bladder neck incision (BNI) or open operation. These operations cost purchasers in the order of £1600–1800, though the real costs may well be higher.

Unfit men who require treatment for retention may be treated by permanent indwelling catheterisation, which carries disposable and nursing costs, which may be high, since the treatment may be continued for long periods.

New technologies include the use of indwelling urethral stents (for unfit men who might have been treated previously by indwelling urethral catheterisation), balloon dilatation, microwave energy, ultrasound therapy, laser treatments and other new devices.

Effectiveness and cost-effectiveness of services

Improvements are seen after treatment with placebo, but α-adrenergic blockers are more effective than placebo and currently cost about £23 per month (*c.* £275 per annum). Finasteride may take up to 6 months to produce maximum benefit and costs £25 per month (£300 per annum). Prescriptions for these agents amounted to 1.5 million per annum in 1997, costing the NHS about £37 000 000. Men who respond to drug treatment may require long-term treatment, which will not totally prevent the need for prostatectomy. Following drug treatment the rates of elective prostatectomy are 4.2% in men treated with finasteride compared with 6.5% in men treated with placebo, and the rates of urinary retention were 1.1% in men treated with finasteride compared with 2.7% in men treated with placebo. Compared with placebo, about 40% of men feel that symptoms improve, but the average degree of improvement is relatively small (symptom scores improve by about 2/35 points more than placebo [17/35 to 14/35] and flow rates improve by about 1.5 ml/s more than placebo [9 to 11 ml/s]). The evidence from drug trials is based on large randomised clinical trials (I-1 evidence), but tight inclusion criteria mean that many men presenting with symptoms would have been excluded from such trials. Drugs and placebo have measurable clinical effects.

Operative treatment by transurethral prostatectomy or open retropubic prostatectomy produces the best improvement, a good outcome being found in about 80% of men (a doubling of flow rates [9 to 18 ml/s] and a marked reduction in symptom scores [from 17/35 to 4/35]), but there are side-effects. One in 1000 men dies as a result of the operation and about 5–10% develop complications such as urinary infection. After eight years, 15% have undergone a repeat operation. The evidence about TURP is based largely on non-randomised trials (II-1), but in most cases has included all patients. The procedure has a moderate to strong beneficial effect (depending on the degree of problems or the presence of complications owing to BPE), but carries risks of complications.

So far as new technologies are concerned, most of these treatments have been assessed in open-phase I/II studies, which have shown a good safety profile and measurable to moderate effects on symptoms, but which have not as yet demonstrated long-term effectiveness. The need for large-scale, long-term randomised trials before such treatments are accepted into the NHS would seem to be obvious. The disposable costs for some of these treatments are up to £500 and the capital costs are also high, at up to £180 000. Some can be performed as a day-case procedure without general anaesthesia, but total NHS costs for many of these treatments have not been fully worked out. Such new technologies can be very capital expensive and indeed often carry recurrent costs for special catheters or probes. The degree of improvement observed is less than that found after TURP. In total, 60% of men report improvement, flow rates change from 9 to 14 ml/s and symptom scores decrease from 17/35 to 8/35. The duration of benefit and the likely reoperation rates are unknown.

Recommendations and models of care

Easy access to an informed GP for all men with LUTS seems to be the key. Initial assessment should be carried out by the GP. Nurse-led prostate assessment clinics staffed by specially trained nurses and overseen by a consultant or committed interested GP might in the future offer an intermediate form of assessment, which may make urology outpatient visits more effective. If GPs are going to manage men with LUTS in primary care by means of drug treatment, they should be confident in their own technique of rectal examination so that they can exclude locally advanced prostate cancer, which can also be a cause of symptoms. Access to a general urology clinic should also be available. Between 150 and 250 per 100 000 men aged over 60 have significant symptoms.

The evidence suggests that men with mild or moderate symptoms without evidence of complications or prostate cancer can be managed by 'watchful waiting'. The evidence also suggests that α-adrenergic blockers and finasteride are more effective than placebo treatments and that in some trials finasteride is less effective than α-blockers. Long-term data have shown that men who have responded to finasteride in the short term and who are kept on long-term treatment have fewer admissions with acute retention or for prostatectomy. However, the number of operations prevented is relatively low. Long-term drug treatment may be provided in primary care.

Men seen in outpatient clinics should undergo clinical history taking and examination; renal function should be assessed and urinary infection and diabetes should be excluded. There is no need for routine intravenous urography or upper tract imaging, but flow rates should be measured and urodynamic studies should be available for selected patients.

Men with acute retention require urgent catheterisation and either urgent admission or urgent assessment by the urologist. Men with chronic retention require urgent outpatient assessment; those with renal impairment need urgent admission. Men with severe symptoms or problems should be referred to the urologist.

Age-specific prostatectomy rates vary widely on a district, regional and international scale. The degree of uncertainty about indications and benefit makes it difficult to provide a recommendation of an optimum rate for prostatectomy. The rate is currently 100 per 100 000 total population (about 10% of the general population are men aged over 60 years).

Outcome measures, audit information and research needs

Treatment is provided for symptoms so the best outcome measures are provided in terms of symptom relief (often measured by specific scores). Objective measures that should be available easily include flow rates and residual urine volumes.

Conventional operative management that is of proven effectiveness includes TURP, BNI and open prostatectomy. New technologies should be used only if they have been or are being formally assessed in the context of a randomised clinical trial.

TURP has been shown to be an effective treatment for approximately 70–80% of men receiving it. The reasons for a poor outcome among the remaining 20–30% may well be due to the fact that not all men with LUTS have bladder outlet obstruction. TURP is likely to be less effective for problems such as detrusor instability or detrusor failure. The surgical treatment of LUTS and the complications of BPE must be viewed within the wider context of the urinary problems of the ageing male and the increasing availability of alternative new technologies.

Audit of TURP has been carried out nationally by the Royal College of Surgeons of England and the British Association of Urological Surgeons. These data have shown, in general, that outcomes have been good, comparable to those published by specialised centres. However, some areas of concern were noted. Some men were not investigated by flow rate assessment, and complications after discharge remain relatively frequent.

Future research needs include good comparative studies of new technologies vs. conventional operative treatments, new technologies vs. drug treatment, and research into the effectiveness and cost-effectiveness of management in primary care.

2 Introduction and statement of the problem

The broad questions that are addressed in this chapter include the following.

- How do men with lower urinary tract symptoms (LUTS) or the complications of benign prostatic enlargement (BPE) present and what is the prevalence of the problem?
- How should men be assessed and managed? What is the role of the general practitioner and what magnitude of service should be provided?
- What is the role of drug treatment?
- What is the role of conventional surgical treatment (prostatectomy) compared with new technology?
- What are the areas of future research needs?
- Is it possible to determine the magnitude of service provision from current data?

The management of men with LUTS comprises a significant proportion of the urologist's workload and the prevalence of benign prostatic hyperplasia (BPH) increases with advancing age.[1–11] However, there is a problem of definition. Recent classifications have emphasised the differences between the following:

- the presence of lower urinary tract symptoms, which may be caused by many problems other than the prostate
- the presence of histological evidence of BPH, which precedes enlargement of the prostate
- the presence of BPE
- urodynamic evidence of bladder outlet obstruction (BOO).

The aetiology of histological benign prostatic hyperplasia

The aetiology of BPH leading to BPE is unknown, but is likely to have an endocrine basis[12,13] in that dihydrotestosterone and oestrogen are essential to the formation of BPH – at least in the dog. Other factors that have been described (but not proven) as positively associated include the intake of dietary fat, sexual activity, alcohol, genetic factors,[2–14] age, a lower socio-economic group, Jewish ethnicity, current non-smoking,[11] daily meat and milk consumption,[15] age, low body mass index, urine pH > 5, and history of kidney X-ray and tuberculosis.[16]

The natural history of lower urinary tract symptoms

The natural history of LUTS is becoming somewhat clearer as some large-scale, long-term community epidemiological studies have now been performed, though in the past investigators have not distinguished clearly between LUTS (symptoms), prostatic enlargement (BPE) and outlet obstruction (BOO). Symptoms and prostatic enlargement both become more common with increasing age. The normal prostate is estimated to weigh 20 (± 6) g at 21–30 years and to remain that size unless BPH develops.[17] By the age of 40 years, histological evidence of BPH is found in 8% of men. This rises to about 90% over the age of 80 years (*see* Table 1, and Table 2 opposite). The early phase of the development of BPH seems to be the most rapid, with a doubling time of 4.5 years for weight between the ages of 31 and 50 years, compared with a doubling time of 10 years between 51 and 70 years of age.[17] The literature suggests that at present a 40-year-old man has about a 20–30% chance of undergoing an operation for LUTS in his lifetime (this has risen from the one in ten chance quoted in the 1970s because of an increase in the numbers of prostatectomies undertaken and the increase in life expectancy).[2,11,18] As indicated above, a 55-year-old man in England has a 25% chance of having a prostatectomy in his lifetime, assuming current NHS operation rates. Studies by Black and the Olmsted County research group have shown that about 25% of men in the community have moderate or severe symptoms, that these symptoms impact significantly on quality of life, and that men with more severe symptoms and problems are more likely to consult a urologist.[19–24]

Table 1: Age-specific prevalence rates (per 10 000) for autopsy evidence of BPH.

Study population	Age (years)					
	< 41	41–50	51–60	61–70	71–80	> 80
Lytton* ($n = 1{,}075$)	800	2,300	4,200	7,100	8,200	8,800
Isaacs and Coffey†						
Microscopic BPH	800	2,200	4,200	6,200	7,900	9,000
Barry‡	800	2,200	4,100	7,000	8,000	8,800
Isaacs and Coffey§ macroscopic BPH	200	800	2,100	3,500	4,400	5,300
Lytton¶ gross histology ($n = 2{,}632$)	–	–	2,360	3,730	3,910	–

* Lytton:[2] figures based on an average of five autopsy studies.
† Isaacs and Coffey:[3] figures based on an average of six studies in Europe, Asia, and approximated from a graph of composite averages.
‡ Barry:[4] figures taken from a graph of a meta-analysis of five autopsy studies of histologic BPH.
§ Isaacs and Coffey:[3] figures based on an average of three studies in England and the USA.
¶ Lytton:[5] based on a study of 2632 autopsies on males over 50 years, using the criteria of gross morphology and histology of sections.

Table 2: Age-specific prevalence rates (per 10 000) for clinical evidence of BPH.

Study population	Age (years)						
	⩽ 54	**55–59**	**60–64**	**65–69**	**70–74**	**75–79**	**⩾ 80**
Watanabe stage 1* ($n = 180/1{,}121$)	270	1,270	1,060	1,580	1,700	2,410	4,170
Watanabe stage 2 ($n = 52/1{,}121$)	0	70	380	490	610	620	1,250
Watanabe stages 1 + 2 ($n = 232/1{,}121$)	270	1,340	1,440	2,070	2,310	3,030	5,420
Gofin† ($n = 217$)	–	–	–	2,800	4,570	5,950‡	–
Lytton§ ($n = 6{,}975$)	800	2,000	–	3,500	–	4,290	–
Lytton¶ ($n = 827$)	260	1,050	–	3,910	–	3,670	1,110
Isaacs and Coffey**	20	1,800	–	830	–	1,900	2,500
Garraway *et al.*††	1,380	2,370	–	4,300	–	4,000	–

* Watanabe[6] used figures taken from a mass screening programme in Japan. BPH stage 1 is an indication for drug administration; stage 2 is an indication for surgery. The combination of stages 1 and 2 gives a prevalence of clinical BPH. Watanabe also cited overall prevalence rates of 18.6% for BPH stage 1, and 5.0% for BPH stage 2, with an average age of 65.2 years, out of a sample of 4,885 screened in 1975–85.
† Gofin[7] studied the health status of 217 elderly men living in Jerusalem. Probable prostatic hyperplasia was inferred from the presence of at least three of the following: frequency of micturition, nocturia, hesitancy, weak stream, terminal dribbling, self-reported prostatectomy.
‡ All over 75 years.
§ Lytton:[5] figures based on men with palpable prostatic enlargement per rectum, derived from 6,975 life insurance examinations.
¶ Lytton:[8] figures derived from records of patients treated in New Haven hospitals for benign prostatic obstruction between 1953 and 1961 (residual urine of more than 75 ml, 82%; acute retention or catheter indwelling, 15%).
** Isaacs and Coffey[3] used the adjusted figures of Lytton *et al.*[8]
†† Garraway *et al.*:[9] age groups specified were 40–49, 50–59, 60–69, 70–79 years. BPH was defined as enlargement of the prostate gland of equivalent weight > 20 g in the presence of symptoms of urinary dysfunction and/or urinary peak flow rate < 15 ml/s and without evidence of malignancy.

Though pathological changes in the prostate can begin as early as the third or fourth decade, symptoms do not usually occur until men are aged 50 years or more.[2] The growth of the prostate gland does not always result in symptomatic problems. Indeed, there is no strong relationship between the size of the gland and obstructive (voiding) symptoms.[6,25,26]

LUTS can be caused by outlet obstruction that is produced by BPE. However, they can also be caused by:

- ageing-related smooth muscle dysfunction
- idiopathic detrusor instability
- neurological disorders such as stroke, cerebrovascular insufficiency and previous transient ischaemic attacks, Parkinson's disease and dementias.

BOO may be caused by BPE or other problems, such as bladder neck dyssynergia. In BOO, there is an increase in outlet resistance, but for some time the bladder is able to increase detrusor contraction and maintain flow under higher pressures.[27] This has been termed 'silent prostatism' and can occur for considerable lengths of time[28,32] If the obstruction continues, detrusor function is affected and symptoms begin to develop. In some men, residual urine is retained, increasing the risk of chronic retention.[27] The cause of acute urinary retention is not known, and it is not possible to predict accurately who will develop acute urinary retention.[29] Men with worse symptoms, who have larger prostates (> 40 g) and who are older (> 70 years) are at increased risk.[30] Acute retention is associated with significantly increased morbidity following TURP.[31]

Studies evaluating drug therapies have reported high levels of spontaneous symptomatic improvement and marked placebo effects.[32–35] However, long-term studies of men who responded well in the short term to finasteride have found that men treated with placebo were significantly more likely to develop retention and severe symptoms requiring prostatectomy.

Symptoms (LUTS)

As mentioned above, symptoms may have a number of causes other than enlargement of the prostate and there are no symptoms that are specific for BPE or BOO.[35] In the past, such symptoms were known as 'prostatism' and were classified into obstructive (now known as voiding) and irritative (now known as storage).[14,36]

Voiding (obstructive) symptoms

These include the following.

- **Hesitancy:** This is a sensation of delay in the onset of micturition. It is the time taken from the initiation of micturition to the commencement of flow. It may last from a few seconds to several minutes. It is a reflection of the time required by the detrusor muscle to generate enough pressure to overcome bladder outlet resistance.[37] It can also be produced by a weak detrusor muscle.
- **Poor urinary stream and/or straining:** Obstruction caused by BPE may develop slowly and so flow changes may occur gradually or even go unnoticed. A measured flow rate of < 10 ml/s is highly suggestive of bladder outlet obstruction, but can also be produced by a weak detrusor muscle.[27,37,38]
- **Sensation of incomplete bladder emptying:** This usually signals the development of residual urine as the bladder is unable to produce enough pressure to overcome the outlet resistance. Similar symptoms, however, can be produced by detrusor instability because the patient's bladder is sensitive to small increases in bladder volume.
- **Terminal and post-micturition dribbling:** At the end of normal voiding, flow ends abruptly. In the obstructed male, the flow may continue at a low level for some time (terminal dribbling).[27] In post-micturition dribbling, the patient thinks voiding is over, only to experience a small leakage some seconds or minutes later, usually resulting in embarrassing staining of clothes. However, these symptoms are not significantly associated with bladder outlet obstruction and may be caused simply by ageing-related weakness in the bulbo-spongiosus muscle, which empties the urethra.
- **Prolonged voiding time:** As the force of the stream is reduced, it takes the obstructed patient longer to void. This may develop gradually or rapidly.
- **Urinary retention:** Some men develop urinary retention. The conventional view is that as obstruction increases and the detrusor becomes less able to compensate, urinary retention can occur. It takes two major forms:
  - *acute retention*: it is commonly held that acute retention requires immediate catheterisation and surgery, but some believe that initial catheterisation should be followed by observing the patient without a catheter, and then making the decision as to whether or not to operate.[39] Acute retention is the reason given for prostatectomy in 20% of men undergoing operation.[27,40]

– *chronic retention*: this can occur over a long period of time asymptomatically, where urine remains uninfected and under low pressure. Patients may have an unnoticed, painless, palpable bladder. Alternatively, they may present with recurrent urinary infections, irritative symptoms (*see* below) or overflow incontinence as the amount of residual urine finally equals bladder capacity, or with more serious symptoms of renal impairment such as nausea, malaise, vomiting and polyuria.[27,41]

Storage (irritative) symptoms

Irritative symptoms are caused when the detrusor becomes unstable and unable to cope with the increased workload caused by obstruction.[14,42] Men with urge incontinence may have increased risk of underlying detrusor instability, which may persist following operations in about 50% of cases.[43]

- **Frequency:** Normal daytime frequency is taken to be less than seven times per day, depending on fluid intake.[27] More frequent micturition can be caused by BPE and BOO producing a small-capacity, irritable bladder, sometimes with associated detrusor instability. In some cases, small volumes of urine have to be voided at frequent intervals, causing some social embarrassment.
- **Nocturia:** This is the sensation of being awoken during sleep by the desire to void. With ageing, nocturia becomes more likely, but in the obstructed male it can become common enough to seriously affect sleeping. As residual urine increases, the frequency of nocturia increases. The use of diuretics or an ageing-related reversal of the normal diurnal rhythm of urinary concentration can produce nocturia.
- **Urgency:** This is the urgent desire to void, usually accompanied by the fear of impending leakage. It is one of the classical symptoms of prostatism, particularly in association with frequency and nocturia. It is commonly associated with idiopathic detrusor instability.
- **Urge incontinence:** This is caused by severe instability, which may be produced by bladder outlet obstruction, but is more likely to be due to idiopathic detrusor instability.
- **Pain:** This is not a symptom of BPE, but may accompany urinary retention, bladder conditions such as bladder stone, and urinary tract infections, some of which may be associated with BPE.

Many of the symptoms associated with BPE are also associated simply with increasing age, and this further complicates the diagnosis of the condition. The evidence that has been collected suggests that large numbers of men may be prepared to accept symptoms of prostatism without seeking help, and that there may also be large numbers of men in the community with undisclosed symptoms.[44]

3 Sub-categories of lower urinary tract symptoms (LUTS) and complications caused by benign prostatic enlargement (BPE)

The clinically important groups or sub-categories of men with LUTS and complications of BPE are based on different use of resources, either because they require more investigation or because they have increased risks of complications and therefore increased lengths of stay.

- Men presenting with straightforward LUTS (60% of men presenting to the urological clinic).
- Men presenting with mixed symptoms (e.g. LUTS plus previous stroke or Parkinson's disease; 20% of men presenting to the clinic).
- Men presenting with retention (25–45% of men who have operations in the UK).
- Men aged over 75 years (30% of men presenting to the clinic).

Men presenting with acute or chronic retention are older and less fit than men presenting for elective prostatectomy. They have significantly longer stays in hospital and have increased rates of post-operative complications and of death.[40]

4 The prevalence of LUTS

Estimates of the prevalence of moderate or severe LUTS are immensely variable, ranging from 5% to 43% in the 65–69 years male age group, depending on the criteria chosen (*see* Table 2). As pointed out above, the term BPH has in the past been used to define benign enlargement of the prostate gland (BPE), the presence of symptoms (LUTS) or the need for drugs or surgery.

Autopsy evidence for histological BPH

Autopsy studies have looked at microscopic and macroscopic lesions in prostate glands.[3] Only a small proportion of men with microscopic lesions will have symptoms of urinary outlet obstruction. Over the age of 80 years, approximately 90% of men will have microscopic histological lesions in their prostates, compared with between 40% and 50% having gross, macroscopic changes (*see* Table 1).

Population survey data

Attempts have been made to measure the prevalence of LUTS (*see* Table 2), but each study employed different definitions, making comparisons difficult. These definitions range from the presence of at least three classic symptoms to a strong indication for surgery. A population survey published in 1991 has suggested that the prevalence of LUTS is higher than has been reported in clinical retrospective and necropsy studies.[9] Certainly the prevalence of LUTS is far higher than historical rates of surgery.[19–24]

The incidence of LUTS and complications of BPE

There is some confusion in the literature about incidence and prevalence.[5] Incidence rates suffer from similar problems of definition, but they are also often based on small samples. Incidence rates of LUTS vary between 5% and 7% per annum in the 65–69 years age group (*see* Table 3). Prostatectomy rates vary between 0.5% and 1.7% per annum (*see* Table 4). The presence of moderate or severe LUTS indicates that there is a huge pool of need not being satisfied. These issues have not been clearly addressed in the literature. Existing evidence about the prevalence and incidence of LUTS is thus fraught with uncertainty. Only those studies that reflect the number of new cases per annum of LUTS registered in a given population are considered here. As with prevalence rates, different authors employ different criteria for determining the presence of LUTS and complications of BPH, and their choices of criteria are not always clear. Rates of follow-up are not always specified. In both the studies cited in Table 3, the process of the 'clinical diagnosis' was not made explicit.

Table 3: Age-specific incidence rates of BPH per 10 000 per annum.

Study population	Age (years)								
	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	> 79
Arrighi *et al.**	95.3	66	158	228	529	523	750	1,080	1,590
Glynn *et al.*† (all men)	37	94	–	313	–	513	–	592	–
Jewish†	–	107	–	443	–	715	–	293	–
Not Jewish†	–	91	–	302	–	476	–	533	–

* Arrighi *et al.*:[10] figures taken from the Baltimore Longitudinal Study of Aging established in 1958. Based on 1057 men in the study who did not have a history of prostatectomy or prostate cancer upon entry to the study and who had at least one follow-up visit beyond the baseline data.
† Glynn *et al.*:[11] figures taken from the Normative Aging Study, based on 2037 men with no surgical treatment for BPH before entry to the study (between 1961 and 1970) to the last examination in 1982.

Table 4: Age-standardised prostatectomy rates, per 10 000 per annum.[45]

Country	Operation rate
England and Wales	9
Norway	9
USA	30
Australia	9

Prevalence and incidence of LUTS and complications of BPE in different population groups

Given the uncertainties mentioned above, it is not surprising that the evidence about prevalence and incidence of LUTS and complications of BPE among different population groups is difficult to interpret,[2,11,45] but on the whole, sample sizes have been small and many important factors such as age, place of birth, socio-economic factors and availability of health services have been ignored or glossed over. There are, however, two findings that have repeatedly emerged from these studies: first, that men of Caucasian origin have much higher incidence and treatment rates than men of Far Eastern/Southern Asian origin[1,2,5]; and secondly, that Jewish men tend to have much higher rates than Protestant or Catholic men[8,11] (*see* Tables 5 to 7 overleaf).

Table 5: Age-specific prostatectomy rates per 10 000 per annum.

Study population	Age (years)								
	40–44	**45–49**	**50–54**	**55–59**	**60–64**	**65–69**	**70–74**	**75–79**	**⩾80**
Surgery*	15.9	13.2	29.2	39.9	142.0	136.0	145.0	244.0	368.0
Surgery† (all men)	–	2.0	–	40.7	–	120.8	–	193.5	–
Jewish†	–	–	–	100.0	–	176.0	–	482.0	–
Not Jewish	–	3.0	–	34.0	–	117.0	–	172.0	–
Surgery‡	–	2.0	–	12.0	–	57.0	–	100.0	109.0

* Arrighi *et al.*:[10] figures taken from the Baltimore Longitudinal Study of Aging established in 1958. Based on 1057 men in the study who did not have a history of prostatectomy or prostate cancer upon entry to the study and who had at least one follow-up visit beyond the baseline data.
† Glynn *et al.*:[11] figures taken from the Normative Aging Study, based on 2037 men with no surgical treatment for BPH before entry to the study (between 1961 and 1970) to the last examination in 1982.
‡ Lytton *et al.*:[8] based on data for men undergoing prostatectomy in three New Haven hospitals between 1953 and 1961.

Table 6: Median age (interquartile range) of men undergoing prostatectomy.[8,10,11]

Operation	Method of admission			
	Elective		Emergency	
	n	Age (range) in years	*n*	Age (range) in years
TURP	20,692	70 (65–76)	6,773	74 (67–79)
Open	1,449	72 (67–77)	773	74 (68–79)

Table 7: Age of men undergoing elective prostatectomy.[8,10,11]

Age group (years)	TURP	Open prostatectomy
⩽ 54	702	20
55–64	4,204	207
65–74	8,632	626
75–84	5,660	497
⩾ 85	675	46

The analysis of treatment variations

There is variation in treatment rates.[45] Explanations for treatment variations are of five broad types: misleading data, differing distributions of disease, differing availability of resources, differing patterns of therapeutic choice, and differing patient perceptions.

Data deficiencies

Deficiencies in the data have been detailed. They include problems of ascertainment, comparability, consistency and comprehensiveness.

Differing distributions of disease

There is no current evidence that age-standardised rates of LUTS and complications of BPE and BOO are likely to differ markedly between differing district populations, e.g. according to ethnic composition. It may be that this simply reflects inadequate information for the UK. For instance, areas with higher Jewish populations may have increased rates, as may areas with more men of Afro-Caribbean origin.

Differing availability of resources

Supply factors are known to influence many treatment rates. Demand for hospital treatments is a complex matter which compounds disease levels, public expectations and referral patterns. One proxy for demand is the waiting list. There is no relationship between median waiting times and prostatectomy rates in district health authorities (now primary care trusts [PCTs]) according to 1989–90 HES data (correlation coefficient $= 0.03$, $p = 0.7$ for TURPs; correlation coefficient $= -0.04$, $p = 0.6$ for open operations).[46]

Differing therapeutic choice

The lack of consensus surrounding definitions of the significance of LUTS and the complications of BPE and its treatments suggests that a large proportion of the variation in surgical rates may be caused by the different therapeutic choices open to individual surgeons. The incomplete explanation of treatment variations under the first three headings supports the contention that differing therapeutic choice is a key factor. This view also emerges from an audit of urological practice[47] and a study of regional variations in Denmark.[48]

Differing patient perceptions

There have not been many studies examining the perceptions of individual men concerning their requirement for treatment of urinary symptoms. It has been shown in a population study published in 1991 that a large proportion of men in the community aged between 40 and 79 years experience urinary symptoms without the desire for treatment.[9] Variations in treatment rates are likely to occur as a result of the different levels of knowledge in the community about treatments for LUTS, and the resulting variability in numbers attending GPs about urinary problems. It is also likely that the differing referral patterns of GPs will contribute to treatment variations. Recent attention of the media to ‘men’s health’ is likely to increase GP consultations and increase referral rates to a urologist.

Incidence of LUTS and complications of BPH according to sub-categories

These are effectively described in Tables 2, 5, 6 and 7. It can be noted for instance that the incidence of symptoms (LUTS) varies according to age. In general in the UK, 10% of the population are men aged between 50 and 65. About 1000/10 000 of this age group (10%) have significant symptoms compared with about 35% of men aged over 65. The incidence of urinary retention is strongly related to age, the size of the prostate and the severity of LUTS, older men (> 70 years) with large prostates (> 40 g) and severe LUTS being at greatest risk. Likewise the incidence of surgery is strongly related to age (*see* Tables 5 to 7). Emergency operations (mainly for retention) are carried out on 25% of men undergoing prostatectomy and occur mostly in older men.

5 Services and treatments available and costs

These include services provided by primary care, urologists in secondary care, drug costs, infrastructure costs and fixed costs in hospitals. The total spend for urological care is not freely available. Information available from informal sources suggests that there are around 100 urological finished consultant episodes (FCEs) per year per 10 000 population (1%). The actual cost of this would be of the order of £80 000 per 10 000 population. Drug costs for LUTS are outlined below. Hospital costs are outlined later, but would be of the order of £23 000 to £37 000 per 10 000 population. One question is whether changing rates of referral and increased management with drug treatment will alter these costs. These effects are modelled later, but the difficulty is the relatively low baseline provision of prostatectomy in the UK, which is heavily predicated on emergency admission with retention. It is therefore likely that increased management of men with LUTS in the community will tap the unmet need rather than markedly reduce the rates of referral and prostatectomy.

The first point of contact for men with symptoms is the GP. The GP will be supported by a range of nursing and professions allied to medicine. Until recently there were few active drugs available for GPs and most men presented late, requiring surgical treatment. In general, therefore, the GP had to decide whether the patient's symptoms and signs warranted reassurance or referral to the urologist at the local district hospital.

Now, however, diagnostic facilities such as ultrasound scanning and flow rate measurement may be available to the GP either locally in the practice or at an open-access clinic in the hospital. Moreover, a variety of drug treatments are now available, including α-adrenergic-blocking agents and 5-α-reductase inhibitors. The GP may wish to assess the patient locally, treat the patient and refer to a urologist only those patients whom they consider require an operation. Another option would be to refer all patients, but ask the urologist to refer back those patients requiring reassurance or drug treatment. Many GPs have not had urological training so may not feel confident about excluding prostate cancer or chronic retention or assessing LUTS and BPE.

Services available at the local hospital will be access to outpatient urological clinics, flow rate tests and other investigations. Increasingly 'hub-and-spoke' services are being set up between smaller local hospitals and larger specialist hospitals (there are models in Newcastle, Middlesbrough and Stockport), which will involve men being assessed locally, but which may involve them having their operation centrally.

None of these different models of assessing and managing men have been fully costed, nor have they been tested for cost-effectiveness of service provision.

The diagnosis of LUTS, BPE, BOO and complications

Diagnosis of BPE is based on clinical history, rectal palpation of the prostate, investigations to search for urinary infection and kidney damage, and some form of urinary flow measurement.[27,42,49] There is no specific symptom pattern that is indicative of BOO – the symptoms of bladder outlet obstruction are the same irrespective of cause[26] – and so the urologist has to eliminate possible malignancies, neurological problems, urethral strictures and calculi, and psychological disturbances before diagnosing bladder outlet obstruction caused by BP.[27]

A major problem in the diagnosis arises from the fact that there is little correlation between the size of the prostate gland and symptoms,[6,25,26] or between reported symptoms and other 'objective' measures, such as findings from urodynamics and scanning.[50] All authors advocate a thorough physical examination to aid diagnosis.

In all cases, a rectal examination of the prostate gland by an experienced examiner is considered essential.[40] The rectal examination allows an estimation of the size of the gland and exclusion of locally advanced prostate cancer (but not exclusion of early prostate cancer in which the gland feels benign). Although not important in terms of diagnosis in relation to symptoms, the size of the gland is crucial in determining the type of surgery to be offered.

Physical examination is required to exclude a palpable bladder (chronic retention) and to check the cardiovascular and respiratory tract, penis, urethra, perineum, anal sphincter tone, rectum, scrotum and testicles.[27]

The assessment of symptoms largely depends on the patient's reporting of them. Some urologists have tried to incorporate standardised questionnaires in their assessments, which focus on the perceived severity of obstructive and irritative symptoms.[10,36,40,49–51,53] Most conclude that these questionnaires need to be used in conjunction with other results because patients find them difficult and because the relationship between symptoms and other more objective findings is uncertain.[50] The most commonly reported LUTS are poor stream and nocturia.[45] Most clinicians rely on a combination of symptoms, an assessment of severity and measurement of flow rates.[26,36,38,50–55] Guidelines for the management of men with LUTS are available in the UK and point out that careful assessment of symptoms and examination is mandatory. Measurement of flow rates is strongly recommended, but urodynamic examination is optional for certain problematic patients because of the risk of producing harm (urinary infections).

Many European urology centres include urodynamic studies in their assessment before invasive treatment is carried out. The reason for this is that men with proven outlet obstruction do best after operation.[56–58,60,61] However, there is debate over how much better men with severe LUTS do compared with men with proven BOO, and in the UK, urodynamic investigations are not strongly recommended.

There is debate as to the usefulness of urodynamics in the management of LUTS. Indeed its use represents another area of controversy.[59] Most urologists now measure flow rates.[56,62] There is agreement that renal function should be assessed by measurement of serum creatinine. There is no indication for a routine intravenous urography (IVU), and many urologists do not image the upper urinary tract at all on the grounds that upper tract tumours and stones are not found more frequently in this group of men.

Prostate-specific antigen (PSA) testing and the exclusion of early prostate cancer

One major current debate is whether men presenting with LUTS should be investigated to diagnose early prostate cancer. There is no evidence that men with a clinically benign gland have an increased risk of prostate cancer. The controversy really is whether men in their fifties and sixties should be screened for early prostate cancer by means of serum prostate-specific antigen (PSA) measurement. This debate is complex.[63] However, current evidence suggests that the guidelines in Table 8 should be followed. Routine PSA screening is not recommended by a UK consensus panel. However, in practice many GPs will have carried out a PSA measurement before referral because of concerns over litigation if prostate cancer is subsequently diagnosed.

Table 8: Guidelines for PSA testing.

PSA testing (category B evidence)
- Is not recommended for routine clinical use
- Is not recommended in men with less than a 10-year life expectancy
- Should only be offered following full counselling of men about the implications

Implications of PSA testing that should be explained prior to testing (category B evidence)
- The test may detect early prostate cancer in approximately 5% of men aged 50 to 65 years
- The test will fail to detect some early tumours
- PSA testing and subsequent treatment of early prostate cancer may incur risk and may not improve life expectancy
- A transrectal ultrasound scan and biopsy, which carry some morbidity, may be needed
- The test may diagnose a tumour which we are uncertain how best to treat

Imaging of the prostate

The prostate can be evaluated by computerised tomography (CT), magnetic resonance imaging (MRI), cystoscopy and ultrasound examination. Experience with CT has proved disappointing for the diagnosis of LUTS, although it can be useful in the assessment of the weight of glands.[42] MRI scans have not proved capable of distinguishing BPE from other conditions.[44] Flexible cystoscopy can provide an easy assessment of the prostate, but its drawbacks are that it requires a local anaesthetic and so is difficult to use routinely, and it increases the risk of introducing infection. Ultrasound has proved extremely useful in the diagnosis of LUTS. The prostate can be scanned transabdominally, perurethrally and per-rectally, and ultrasound can also represent internal details of the prostate.[42] The most convenient method is through the per-rectal route, from which the weight of the gland can be estimated. There is no indication for imaging the prostate routinely in men with LUTS.

Summary of assessment of LUTS

The diagnosis of LUTS is a residual diagnosis, which is applied after other conditions such as malignancy, neurological disturbance, infection and so on have been excluded. The diagnosis can include a wide range of urinary symptoms and involve a wide range of tests, depending on an individual clinician's preferences and beliefs. It is important to note that the diagnosis of LUTS does not necessarily lead to a requirement for treatment because of the variable nature of the natural history, particularly the tendency for spontaneous remission and the wide-ranging levels of tolerance of symptoms by individual sufferers.

Treatments

Following assessment and diagnosis, the major types of non-operative treatment include:

- reassurance and discharge
- 'watchful waiting' and conservative treatment
- drug treatment, including α-adrenergic agents or 5-α-reductase inhibitors.

The major operative treatments include:

- open prostatectomy (retropubic prostatectomy; RPP)
- endoscopic or transurethral prostatectomy (TURP)
- transurethral incision of the prostate (TUIP; sometimes described as bladder neck incision or BNI)
- various new technologies.

Urologists treat LUTS rather than histological BPH or BPE[64,65] (i.e. a combination of symptoms and low urinary flow rates) because symptoms of obstruction are not related to the size or development of the prostate gland. It has been suggested that there may be three principal stages of treatment: drugs for early symptoms, prostatectomy for complications and advanced symptoms, and a catheter for men with severe comorbidity.[6] Currently, the most common treatment option is prostatectomy, with drug therapies typically being used before surgery. Permanent catheterisation is used primarily in patients considered unsuitable for surgery.

The aims of surgical treatment are to remove outlet obstruction, restore easy and comfortable micturition and prevent the progress of renal damage.[26] BPE can lead to irreversible renal insufficiency and thus death,[6] but this is very rare. Patients may be admitted for an emergency prostatectomy as a result of acute urinary retention. The literature suggests that approximately 25% of men undergoing TURP in the UK are admitted with acute retention.[25,65] A further 15% are admitted with chronic retention. The majority of patients are therefore treated electively for their urinary symptoms.

'Watchful waiting' and conservative treatment

'Watchful waiting' can essentially be defined as careful assessment and reassurance and then arranging to review the patient. A more active approach can be beneficial. This includes giving general advice about the timing of fluid intake and the adoption of postponement of mictutition with the aim of decreasing symptoms of frequency and urgency. The use of pelvic floor exercises can also be of help. There is little literature on this topic but this approach is cheap, can be effective and perhaps should be more widely used before resorting to drug treatment. A randomised prospective clinical trial performed by Wasson and his colleagues has confirmed that 'watchful waiting' is safe, and can be effective for some men with moderate symptoms, but that it has a higher failure rate than TURP.[66,67]

Drug therapies

There are two basic types of drug therapy in the treatment of LUTS, including α-adrenergic antagonists and inhibitors of 5-α-reductase. Other agents such as phytotherapeutic substances (e.g. saw palmetto extract) are more widely used in Europe, and in a meta-analysis[68] were shown to be effective.

Alpha-adrenergic antagonists or blockers

These drugs cause the relaxation of the smooth muscle of the prostate.[14,25] They thereby relieve temporarily the symptoms of outlet obstruction, but do not affect the size of the gland and so are not always effective for long periods of time.[25,69–71]

Hormonal therapies

The importance of hormones in the development of BPH and BPE is the subject of debate, but as it seems clear that intact testes and ageing are necessary for its development, the blocking of androgens has interested some authors. Castration has been shown to cause the regression of BPE after about three months, by shrinking the prostate gland.[34] The treatment has gone out of favour, however, because of its side-effects of loss of libido and potency.[14,30,35,71,72] Finasteride is an agent that blocks the conversion of testosterone to dihydrotestosterone.[13,35] This treatment is safe and is more effective than placebo.

Prostatectomy in the treatment of LUTS and complications of BPE

The aim of a prostatectomy is to remove the inner tissue of the prostate, leaving the outer caudal capsule.[65] There are two basic methods of prostatectomy: open and transurethral. Open surgery can be done by three routes: perineal, suprapubic and retropubic. Pioneered in 1909,[73] TURP increased in popularity from the 1960s with the development of the resectoscope. It is now the most common form of treatment, although in recent years there has been some controversy about its long-term safety and effectiveness (*see* below). Resection of an average 30 g gland is reported to take a specialist urologist about 15–20 minutes.[65]

Prostatectomies can be performed with general, spinal or local anaesthetics.[74,75] Spinal anaesthesia is preferred in patients with cardiovascular or respiratory problems, and reduces blood loss.[70] Prostatectomies are now carried out by specialist urologists. Open prostatectomy, the enucleation of the adenoma of the prostate gland for BPE, has been performed on a regular basis for over 100 years.[76] With the advent of the transurethral resection technique, open prostatectomies are now principally indicated for large glands that are difficult to resect or for patients with osteoarthrosis of the hips, which prevents their being positioned correctly for resection.[77]

The most common open approach is the retropubic route, which allows a clear view of the prostatic cavity and an easier convalescence for the patient.[26,77,78] The catheter is removed from retropubic patients after three or four days (six to seven for transvesical), and so the patient requires a 5- to 10-day stay after open surgery.[76]

Transurethral resection of the prostate is the hallmark of the specialist urologist.[77] Some 400 000 TURPs are carried out per annum in the USA.[78] In the UK, 42 000 were carried out in NHS hospitals in England in 1989–90. It is the most common operation performed by specialist urologists, with around 98% of their prostatectomies now TURPs.[26,77] NHS data show that in 1989–90, 93% of all prostatectomies were TURPs. TURP is the tenth most frequently performed operation in the USA, and the second most common reimbursed under Medicare.[78] Urologists in the UK carry out a mean of 67 TURPs per annum. It is known as the 'gold standard' for the treatment of BPE.[79] TURP is considered to be the best treatment for most patients, with a low mortality rate at around 0.4% for elective operations.[80] TURPs can be performed using general, spinal or local anaesthesia. Patients have to be catheterised after the operation for about 48 hours, so it is not possible to do TURPs on a day-case basis. More than 90% of prostatectomies are performed transurethrally. Estimating the population requirement for prostatectomy is very difficult because of the uncertainty surrounding the definition of the condition. In practice, however, around 40 000 operations per year are carried out in England and Wales, which means that about one man per 1000 of the population base (male and female) requires this operation per year. Increasingly, a number of men are being treated by new technologies.

Indications for prostatectomy or new technologies

Absolute contraindications for a prostatectomy are few and it is becoming rare for patients to be considered unfit for a prostatectomy.[78] As Miller stated in 1965, 'if a patient is requested to "get out of bed, walk round it, and get back again" and he can comprehend this and then do it, we can get him through a prostate operation'.[81] It is considered that gross mental disturbance and a life expectancy of less than six months are the clearest absolute contraindications.[26] Relative contraindications include renal failure, extreme age, diabetes, cardiovascular and cerebrovascular disease, and respiratory failure.[34,65,82,83] These relative contraindications can increase the risk of mortality by between 3 and 15 times.[34,84] Age alone is not considered to be a clear contraindication to surgery, but the reduced capacity for adaptation in the elderly, particularly in the cardiovascular system and altered pharmacokinetics have to be taken into account.[85] One study reported an 80% success rate with patients over the age of 80 years.[86] Very high-risk patients may be given long-term catheterisation as an alternative to surgery,[34] but this is very much a last resort. There have been steady reductions in overall morbidity and mortality rates following prostatectomies, but they have remained the same for high-risk patients.[87]

Although useful as a starting point, the classification shown in Table 9 and Table 10 (*see* overleaf) does not specify volumes or rates, nor does it explain what is meant by 'symptoms (severe > moderate)', which could thus be interpreted variably. Table 9 shows the American Urological Association clinical indications for TURP.[59] Table 10 shows Christensen and Bruskewitz's suggested three levels of confidence for indications for intervention in LUTS and complications caused by BPE.[29]

Table 9: American Urological Association clinical indications for TURP.[29]

A patient who is a reasonable surgical risk with one or more of the following:

1 urinary retention due to prostatic obstruction
2 intractable symptoms due to prostatic obstruction
3 recurrent or persistent urinary tract infection related to prostatic obstruction
4 a patient who is a reasonable surgical risk with two or more of the following:

A documented post-voiding residual urine
B pathophysiological changes of kidneys, ureters or bladder caused by prostatic obstruction
C abnormally low urinary flow rate or a normal flow rate, but with an abnormally high voiding pressure secondary to outlet obstruction

Table 10: Indications for intervention in BPH.[29]

Strong
- azotaemia (with hydronephrosis)
- overflow incontinence
- high post-voiding urinary residual (volume not specified)
- urinary tract infection (recurrent, with increased residual)
- severe haematuria

Moderate
- acute retention (recurrent > single episode)
- symptoms (severe > moderate)
- increased post-voiding residual urine (volume not specified)
- reduced maximum urinary flow rate (rate not specified)

Weak
- cystoscopy findings (trabeculation > 'visual obstruction')
- prostate size

New technologies used in the treatment of LUTS and BPE (*see* appropriate tables)

Balloon dilatation

Balloon dilatation has been used as an alternative to prostatectomy. It is very similar to the operation of angioplasty done for coronary artery disease. A balloon is placed into the prostatic urethra by either visual or finger guidance and it is then inflated. This has the end result of tearing the prostate gland (usually anteriorly) and creating a wider channel. No prostate tissue is removed and the procedure does not work well for large prostates. It is not now recommended.

Prostatic stents

Stents are wire devices, shaped like small springs or coils, placed in the prostatic urethra. They are generally placed under local anaesthesia and require about 20 minutes to fit. Their use has in general been reserved for patients thought to be medically unfit, although some centres fitted them in men with severe symptoms while they were waiting for an operation. Given our present knowledge, this approach is difficult to support. Major problems with stents concern the irritation and debris that form on the stent, as well as a higher incidence of urinary tract infections. A number of types of stents have been used. Some (e.g. Memokath) are made of metal whose shape is thermostable so that they can be fitted while they are malleable, and then at body temperature their shape reverts to the original coil. Other stents (e.g. Urolume) become incorporated into the wall of the urethra over time, which makes them difficult to remove. Most authors would reserve the use of stents for the very unfit who would otherwise be fitted with a permanent catheter. The evidence that has been produced by a large number of small observational studies suggests that most types of stent can be successful in the treatment of men unsuitable for surgical treatment because of comorbidity and whose only alternative is seen to be an indwelling catheter. There are no data to support the notion that this treatment might be effective in treating a wider range of men with BPH, or that stents are a suitable treatment for men currently on the surgical waiting list.

The various type of stents include the following:

- temporary stents, including the Nissenkorn catheter, which is positioned under local anaesthesia. It can be removed through a lubricated urethra by a pull-cord. Other stents include the Prostakath, which is an intraprostatic spiral. It is gold-plated to minimise encrustation
- second-generation temporary stents, made of nickel–titanium alloys that are flexible and expand when heated, but are malleable when cool. The most common type is the Memokath
- permanent stents, which become covered with epithelium within the urethra. These include the Urolume, Wallstent and ASI titanium stent.

High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) is delivered to the prostate via a transrectal probe and causes prostatic lesions without damage to the rectal wall or other tissues. It is still at a developmental stage, but does have promise for future use.

Microwave therapy

Heating of cells using microwaves to 42–44°C destroys malignant tumour cells, but normal cells are destroyed only at temperatures in excess of 50°C. The rationale is that heat will destroy benign tissue, although this has not been proven. Three basic modalities of tissue destruction can probably be described: hyperthermia (40–45°C), thermotherapy (46–60°C) and thermal ablation (61–75°C).

Early treatments heated the prostate to about 42–46°C and were known as hyperthermia. The energy was applied per rectum or per urethra. Although there were some symptomatic improvements, no objective evidence of destruction of prostatic tissue could be confirmed.[88]

Later machines were fitted with more sophisticated methods of controlling rectal and urethral temperature and heated the prostate to >45°C. They may produce more tissue damage and greater effects on symptoms and flow rates. This is known as thermotherapy. The situation is even more complex because later machines provide even greater energy and the treatment is known as high-energy thermoablation.

Microwave hyperthermia

Transurethral microwave therapy involves an ultrasound generator and receiver which converts the energy into heat, which is focused on the centre of the prostate lobes. The amount of energy determines the degree of heating. Hyperthermia results in very little tissue damage as measured by changes in serum PSA. No prostate tissue is removed for pathological diagnosis.

Microwave thermotherapy

The new-generation microwave machines use a catheter that cools the lining of the prostatic urethra while the prostate tissue deep inside is heated.

Laser therapy

Laser therapy, using a neodymium:yttrium-aluminium-garnet (Nd:YAG) laser, was first used in the treatment of BPH using bare fibres, but with disappointing results. Later special probes were used, which resulted in discrete lesions being produced within the prostate. Another development is transurethral ultrasound-guided laser-induced prostatectomy (TULIP), which combines a standard Nd:YAG laser with a TULIP device, which fires the laser beam through a water-filled inflated plastic balloon at a 90° angle (side-firing) near the end of a probe.

With laser therapy, patients are typically catheterised for several days following treatment, while tissue sloughs. Improvement in symptoms and flow rates is reached after approximately six weeks. The laser is a source of high energy that has gained much attention as a unique surgical tool. In urology, the light energy is converted to heat on contact with tissue to produce its surgical effect. It is an energy modality utilised in breaking stones, treating bladder tumours and removing prostate tissue.

Several types of laser treatment have been used to treat men with BPH. Initially rather non-specialised probes were used to vaporise tissue, but the rate of tissue destruction was so slow as to limit their use to carrying out a bloodless bladder neck incision of TUIP. The next development was a contact laser probe, which resulted in tissue destruction but not vaporisation using an Nd:YAG laser. This is known as visual endoscopic laser ablation of the prostate (VLAP or ELAP). Recent developments include the use of hybrid lasers using Nd:YAG plus high-power potassium titanyl phosphate (KTP), which result in the destruction of larger volumes of prostate.

TULIP has also been used, as has interstitial laser therapy (ILP), but no large-scale trials have been reported. The next development is likely to be holmium laser treatment used to dissect out the prostatic adenoma, which is then pushed into the bladder where it can be morcellated transurethrally or by placement of a suprapubic tract. The advantage of this technique is that large amounts of adenoma are removed, which is likely to result in better long-term outcomes compared with other minimally invasive methods.

In general, laser treatments have resulted in improvements in symptoms and flow rates only a little inferior to conventional TURP. However, no long-term randomised studies have been done to allow us to determine whether these treatments should be introduced into routine clinical practice.

Transurethral incision of the prostate (TUIP)

TUIP is a long-standing, simplified alternative to TURP that simulates its results in both symptom relief and flow rate improvements. The procedure is performed by making a simple, deep cut or incision along the entire length of the prostate to split it open. This allows the circular muscle fibres running around the prostate to spring open and increase urinary flow by opening the prostatic urinary urethra. TUIP is ideally suited to smaller prostates and has a lower incidence of retrograde ejaculation. In appropriately selected patients with relatively small and anatomically appropriate prostates, the success rates for TUIP are similar to those for TURP, with the advantage that hospital stays and recovery are much shorter. Large-scale, long-term trials have not been done.

Transurethral electrovaporisation of the prostate (TVP)

A new modification of TURP is transurethral electrovaporisation of the prostate (TVP). Essentially, this technique uses a grooved roller-ball to apply electrical energy to vaporise the prostatic tissue. Compared to the standard TURP, the procedure results in less bleeding, shorter hospitalisation and catheter times, and a faster recovery period.

The procedure allows the grooved roller-ball electrode to rapidly heat the tissue to turn it into steam, leaving a space where the prostate tissue was previously present. The majority of heat is dispersed by a constant flow of water. The defect does not bleed because it is coagulated and sealed by the roller-ball electrode. However, large veins may still bleed and reports of late rebleeding following separation of slough have appeared. Technically, this is a new way to do a TURP, and TVP can also be utilised to perform a TUIP.

Transurethral needle ablation of the prostate (TUNA)

This technique involves the application of radio-frequency current through small needles placed bilaterally into the prostate gland via a transurethral approach, to induce tissue destruction by local heating. It can be performed with minimal anaesthesia and as an outpatient procedure. Preliminary data on a small series of patients suggest it has the potential to be a viable, minimally invasive surgical alternative for the treatment of BPH. The amount of tissue destruction is likely to be small and to limit the size of gland treated by this technique.

Conclusions about new technology

There are serious problems with many of the studies of new technologies. Initial phase I studies looking at safety are done well, as are the non-randomised studies showing safety, side-effects and effectiveness. However, randomised studies are in general small and short term, which has not allowed proper comparison with conventional treatment. Cost-effectiveness has not usually been calculated. Moreover, the generalisability of many of the trials is uncertain.

Costs

It is often assumed that a certain proportion of men currently treated by surgery could be managed by 'watchful waiting'. However, in many instances this approach has been practised for many years by the patient and GP. In addition, the advent of medical therapy will be likely to delay referral to the urologist. Data suggest that a small number of men will be saved prostatectomy by this approach.[85]

The cost of provision of treatment for BPH is considered here.

General practice

A visit is estimated to cost £15. The attendance rates per year to the GP in connection with BPH are not entirely clear, but would be of the order of 5% of men aged over 60 (who represent about 10% of the average practice). Therefore 0.5% of the total of the GP's patients will present each year. In a population of 10 000 people there will be 1000 men aged over 60 years. Fifty will go to see their GP each year, 20 will be reassured or treated by 'watchful waiting', 20 will be referred for assessment to hospital (10 of these will undergo operative treatment) and 10 will be managed by drug treatment.

Initially, the cost of providing the present average level of care is calculated. This is divided into costs falling on general practice, costs falling on the hospital sector of the NHS, and costs of private care (which will fall on both the general public and the insurance companies). These calculations are rather simplistic and it is likely that the true costs are much higher. For instance, the treatment of LUTS and BPE will cost around £40 000 per annum, most of the costs falling on the hospital. However, these costs are likely to be 'subsidised' by other, more minor procedures. Fixed overheads are significant. It is likely that costs would be double in these estimated costs.

Two alternative calculations are then made. First, it is assumed that 20% of those currenty treated by surgery will be subject to 'watchful waiting' rather than immediate treatment. 'Watchful waiting' is assumed to consist of the initial two visits to the outpatient department, plus a further two visits per year, making a total of four visits in the first year. When notice is taken only of the change in costs in the present year, it appears that resource use is much reduced. It is, however, apparent from a more detailed consideration that the cost of 'watchful waiting' will have costs in future years that will not be incurred where operation takes place in the current year.

Second, it is assumed that there is an increase of 25% in the number of patients receiving surgery. It appears that this course of action will lead to an increase in cost to the NHS. However, although not explicitly calculated, it is likely that some of this cost will be offset by a reduction in costs of emergency operations and further consultations for these same patients.

(i) Costs per 10 000 of the total population (per 1000 men aged over 60 years)

GP costs – 50 men			
20 referred – NHS	1 visit	@ £15	£300
4 referred – privately	1 visit	@ £15	£60
26 not referred	3 visits	@ £15	£1,170
NHS hospitals – 20 referred			
10 treated medically/untreated	2 outpatient visits	@ £100	£2,000
10 prostatectomies	3 outpatient visits	@ £100	£3,000
	Operation	@ £1,600	£16,000
Private hospitals – 4 referred			
3 operated on:	2 outpatient visits	@ £120	£720
	Operation	@ £2,500	£7,500
1 not operated on	1 outpatient visit	@ £120	£120
Total expenditure on BPH			
GP	£1,530		
NHS hospital	£21,000		
Private hospital	£8,340		
Total	**£40,870**		

(ii) Change in NHS cost based on the assumption that 20% of those currently treated by surgery will now be treated by 'watchful waiting'

NHS hospitals – 20 referred			
6 treated medically/untreated	2 outpatient visits	@ £100	£1,200
4 treated by 'watchful waiting'	4 outpatient visits	@ £100	£1,600
8 prostatectomies:	3 outpatient visits	@ £100	£2,400
	Operation	@ £1,600	£12,800
Total NHS hospital expenditure			**£18,000**

It may be suggested that much of the 'watchful waiting' costs could be transferred to general practice. However, the situation is complex because many GPs are already practising 'watchful waiting' on men who are never referred. The referral takes place because of the other complexities, such as worse symptoms, or other conditions, such as strokes or Parkinson's disease. While such men may be referred back to the GP, it is likely that one or two further visits to the urologist will be indicated to ensure that this policy is correct. The above figures show an apparent saving of approximately £3000 for the NHS hospital resulting from the reduction in the number of prostate operations and the increase in 'watchful waiting'. This policy will, however, lead to an increase in costs in further years as the 20% of patients referred to the 'watchful waiting' (medically treated) group are observed regularly. If it is assumed that these patients are observed in outpatient departments every six months over a five-year period, this would lead to a cost of £200 per person per year. This is just the cost of 'watchful waiting', and does not include the costs of operating on any patients requiring a prostatectomy during the period of 'watchful waiting'. It also does not include the costs falling on patients who decide to opt for an operation in the private sector. The analysis is thus, in a sense, incomplete. It does, however, show the importance of considering all aspects in changes in policy.

(iii) Change in NHS cost based on the assumption that there is an increase of 20% in the number of patients receiving surgery

NHS hospitals – 20 referred

8 treated medically/untreated	2 outpatient visits	@ £100	£1,600
12 prostatectomies:	3 outpatient visits	@ £100	£3,600
	Operation	@ £1,600	£1,200
Total NHS hospital expenditure			**£24,400**

The figures in section (iii) show an apparent increase in costs of £3400 for the NHS hospital resulting from the increase in the number of prostate operations and the reduction in 'watchful waiting'. However, just as a reduction in the number of operations caused changes in future resource use, so the policy of increasing operations is likely to have future effects. In particular, it is likely that there will be a reduction in future resource use as patients no longer need to be observed at future consultations.

Again, it should be stressed that in this model no consideration is given to changes in the benefit received by the patient. It is not, therefore, possible to determine the most cost-effective option for districts to pursue. In addition, the considerable uncertainty surrounding many aspects of the model, and the poverty of the data used, mean that the model should not be used to draw sweeping conclusions.

6 Effectiveness and cost-effectiveness of services

The effectiveness of treatments for LUTS and BPE

The evidence is that in England and Wales, men wait for a number of years before visiting their GP. The advent of medical treatments has meant that a further period of treatment with these agents then takes place. Some men respond well to 'watchful waiting' or medical treatment and do not require referral to hospital. The increasing publicity about prostate diseases is likely to result in more men going to their GP earlier.

New technology has also meant that fewer men proceed straight away to prostatectomy, although there have been few direct comparisons by means of randomised controlled trials (RCTs).

Drug therapies and their effectiveness

Alpha-adrenergic antagonists or blockers

Clinical trials of phenoxybenzamine showed it to be effective, but to have unacceptable side-effects.[35] Other drugs are currently being tested, and it is hoped that multi-centre studies will clarify the precise role of α-adrenergic antagonists in the treatment of LUTS.[35] The role of drugs has been reviewed in a systematic review. Recent drugs include alfuzosin, terazosin and tamsulosin, which are more 'prostate selective'. These α-selective agents are more expensive and appear to have fewer side-effects than the older agents. In addition, some can be given as single-dose treatments. The side-effects include postural hypotension, dizziness, nasal stuffiness and headaches. Modern drugs are more selective for α-1 receptors and some can be given as single doses per day, which may offer improvement with compliance.

Hormonal therapies

Finasteride is safe and is better than placebo, but may be less effective in smaller glands (< 30–40 g).

Studies evaluating drug therapies have reported high levels of spontaneous symptomatic improvement and marked placebo effects.[33,34] One study suggested that 60% of patients may get better on a placebo drug, and another that more than one third of untreated men with symptoms of urinary obstruction caused by BPH experienced a spontaneous improvement based on subjective criteria and a 20% improvement according to objective findings.[69–71] It has been suggested that drugs have been administered in incorrect doses and over too short periods of time to show their true effectiveness but, on the whole, drug therapies have so far been limited to providing temporary relief for those who do not want surgery or are awaiting a prostatectomy. One paper suggested that finasteride was less effective than α-blockers, but this agent may be less effective in smaller glands (< 40 ml) and this trial did contain rather more patients with smaller glands than might usually have been expected.[71] Two years on, men taking active treatment had lower rates of prostatectomy (89 of 2113 [4.2%] vs. 138 of 2109 [6.5%]) and of retention (24 of 2113 [1.1%] vs. 57 of 2109 [2.7%]). However, 36% of men reporting retention (45/126) and 21% of men reporting surgical intervention (60/287) were excluded from this study. Though the trials were large and differences significant, the number of events prevented (49 prostatectomies and 33 episodes of retention) was small. The cost of drugs would have been over £1.6 million while the NHS cost of treating these 82 events surgically would have been no more than £200 000. While more men may benefit in the forthcoming years from drug treatment, so will the cost of drug treatment increase.

The effectiveness of prostatectomy

Information about the effectiveness of prostatectomy is hampered by lack of knowledge about the natural history of LUTS and the likelihood of spontaneous improvement. Prostatectomy has been the treatment of choice because it has been assumed to relieve the symptoms of urinary outlet obstruction. Studies have suggested that 75–90% of men improve after a TURP,[77–79] and that 79–90% are satisfied with the results.[89] It is thought that the most severely affected individuals experience the greatest levels of success; more than 90% of severely and nearly 80% of moderately symptomatic individuals can expect to improve after a prostatectomy.[90] There have also been studies that have examined the failure rate of prostatectomies. Failure rates range from 2% to 35% for TURP,[91–99] and were 0% in the only study to look at open procedures.

Prostatectomies are associated with some post-operative complications. Studies mentioning complications are presented in tabular form opposite so that they can be compared (*see* Tables 11 and 12).

Some complications occur following both TURPs and open prostatectomies. Both have relatively low operative mortality rates, ranging from 0 to 2.1%,[100–120] slightly higher for open procedures than TURPs. The most common cause of death after TURP is cardiovascular complications. One of the most common post-operative complications is a urinary tract infection, occurring in 4–63% of cases. Urethral strictures have been found in approximately 1–29% of cases.

Several complications are shown in the literature to occur only in men having TURPs. A syndrome has been documented (called TUR syndrome) that is characterised by a rise in blood pressure, bradycardia, mental confusion, nausea, vomiting and visual disturbance, thought to be caused by intoxication with the

Table 11: Complications (%) of open prostatectomies (quoting papers with population figures).

Reference number	93	98*	98†	25†
Number of operations	53	621	223	98
Complications (%)				
Urethral strictures	3.8	–	–	–
Urinary tract infections	51	19.3	4	38
Incontinence	0	–	–	–
Pulmonary infection	11.3	–	–	–
Operative mortality	0	2.1	0.9	–
90-day mortality	–	0.6	0.5	–

* Suprapubic route.
† Retropubic route.

Table 12: Complications (%) of TURPs (quoting papers without population figures).

Reference number	98	103	108	110	111	25	105	101
Complications (%)								
Urethral strictures	–	1–29	–	–	–	–	–	–
Urinary tract infections	–	–	–	–	–	–	–	5–63
TUR syndrome	–	–	–	–	–	–	2–7	–
Incontinence	–	–	3	–	–	1–3	–	–
Impotence	10	–	–	16–30	4–40	< 13	–	–
Retrograde ejaculation	50	–	–	–	–	–	–	–
Operative mortality	0.4	–	–	–	–	0.2	–	–

irrigating solution.[105] Incontinence has been reported in a small proportion of cases (3%) immediately post-operatively,[108] although the problem can rectify itself, and only 1% of these patients have to undergo further surgery to correct incontinence. Impotence has proved much more difficult to evaluate.[109] The TUR procedure results in the bladder no longer being shut off from the prostatic cavity, and this can lead to dry or retrograde ejaculation in many cases (between 11 and 100%). Figures for impotence also vary among studies (between 0 and 40%).[109–111] TURPs are generally associated with a deterioration in various aspects of sexual expression,[109] but this should not necessarily occur. Some of these post-operative problems are thought to be caused by involuntary erections during the resection procedure, which cause the surgeon to resect incorrectly.

Some men are more likely to have poorer outcomes than others. These tend to be men with the smallest prostates and low voiding pressures, weak detrusor function or bladder muscle instability and urge incontinence.[113,114] These men are more likely to have a TURP than an open prostatectomy, and perhaps to undergo more than one procedure.

Work in the late 1980s by Wennberg *et al.* reopened the debate about the outcomes and effectiveness of TURPs compared with open surgery.[115–117] Up to 1987 it was generally accepted that TURP was the most effective operative procedure for men with relatively small glands, and that TURPs could be used electively as a solution to embarrassing symptoms. TURPs had largely replaced open prostatectomies in most modern health systems. Roos and Ramsey analysed the outcomes for prostatectomy in Manitoba, Canada, over an 8-year period. They showed that post-operative mortality rates were similar to or higher for TURPs compared with open surgery, and that reoperation rates were much higher (16.8%) for TURPs than for open prostatectomies (7%).[98]

Wennberg's team followed this with a study comparing men undergoing TURP and open prostatectomy in Denmark, in Oxfordshire, UK, and in Manitoba, Canada over eight years.[115] This showed that the cumulative percentage of patients undergoing a second prostatectomy was substantially higher after TURP than open prostatectomy (12.0 vs. 4.5% in Denmark, 12.0 vs. 1.8% in the UK, and 15.5 vs. 4.2% in Canada). It also showed that long-term age-specific mortality rates were higher for TURP than open prostatectomy.[110] Other studies confirmed the finding of higher death rates and reoperation rates for patients having TURP.[111,112] A rate of 2.0–2.8% per annum for recurrences has been suggested. Another study in Denmark also found that the risk of dying within 10 years of a prostatectomy was significantly higher for TURPs than open procedures, with the most common cause of death being chronic bronchitis.[118] This debate is somewhat sterile because it has been shown that men undergoing TURP are less fit than men undergoing open operation and that men who undergo open operation have significantly increased life expectancies compared with control populations.[119]

The other major question of effectiveness concerns the rate of reoperation. After eight years, 12–18% of men who had had a TURP required a repeat procedure. This indicates an excess risk of three to five times that of open surgery.[98,115] It may be that many TURPs may not be complete, although this is usually denied by urologists. There is little evidence of major differences in the symptomatic and urodynamic outcomes of the two procedures, although peak urinary flow is reported to be higher in open prostatectomy, implying that it is more complete. It is suggested that it is more likely that a surgeon will operate on a borderline case using the transurethral procedure, and this may contribute to the increased numbers of reoperations.[103] It is not known, however, why men required repeat procedures – whether for more complete resection, persistent symptoms or because of more severe symptoms resulting from the iatrogenic effects of the first procedure. Further research is required to determine the reasons for the high revision rate, and in the UK, improvements need to be made to routine health service data so that issues such as late mortality and repeat procedures can be investigated.

Other therapies in the treatment of LUTS and BPE

Minimally invasive procedures

Balloon dilatation (*see* Tables 13 and 14[120–129])

Recent studies have demonstrated that most patients who undergo balloon dilatation have recurrence of their symptoms relatively soon afterwards and require repeat treatments within two years. With the availability of more efficacious minimally invasive treatments, balloons are less acceptable. No large-scale controlled trials have been reported. In some of the uncontrolled studies, men were stated to be unfit for prostatectomy and might otherwise have been treated by catheterisation. However, some studies recruited a large number of patients over a short time and the definition of lack of fitness was not explicit. This criticism also applies to many studies of prostatic stents. Other studies recruited men at the other end of the symptomatic spectrum, taking those with only mild symptoms (who now are most likely to be managed by 'watchful waiting' or with α-blockers).

Conclusions on balloon dilatation

Balloon dilatation has been shown to be safe, and results in some symptomatic improvement in some patients with LUTS, but whether it is better than placebo remains uncertain. The exact mechanism of this improvement is unknown. Morbidity following the procedure is low, particularly for epididymitis, urinary

Table 13: Results for non-controlled trials of balloon dilatation.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Marks[126]	43	59.6	9.8	15.7		77%			73%
McLoughlin[127]	54	74	9			51%			
Moseley[128]	77	64.4	24	16 (approx.)	4	91%	8	15	
Renfer[129]	27	66	12	17.3	10	42%	11.5	14.3	24%

Table 14: Results for controlled trials of balloon dilatation vs. TURP, TUIP and observation.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score before	Symptom score after	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Chiou[121]									
Balloon	16			15 (Madsen)	3.4	77	8.3	12.8	54
TUIP	14			15.4	4.2	73	9	18.1	101
Donatucci[124]									
Balloon	20		18	14.1 (Madsen)	7.3	49	11.8	16.1	36
TURP	18			13.6	7.7	43	12.2	19.8	62
Klein[125]									
Balloon	5	60.2	24						
Observation	3	60.3							

tract infection and incontinence, but mortality rates are high (3.5%), probably due to the numbers of high-risk patients treated. Studies indicate poor long-term results from balloon dilatation – with a cumulative failure rate at five years of 32% (90% CI: 15–52), and with a high proportion of failures tending to occur in the first year (*see* Tables 13 and 14).

Prostatic stents (*see* Table 15[130–136])

The studies shown in Table 15 have been mostly carried out in patients with acute or chronic retention. In general, the short-term success rates have been about 60%, the other 40% requiring stent removal and catheterisation. The rates of complication (such as haematuria, encrustation, displacement and blockage) in men fitted with temporary stents are not clear because large-scale, long-term results have not been published, but many short-term series report that up to 25% require their stents to be replaced or resited. Similar problems apply to review of permanent stents, but certainly some cause encrustation and calcification and may require open surgical removal, which is technically difficult.

High-intensity focused ultrasound (HIFU) (*see* Table 17[137–140])

Early results indicated that this therapy was well tolerated. Most patients suffer from transient retention and haematospermia. Therapy resulted in an increase in maximum flow rate, and reduction in both residual urine and American Urological Association (AUA) symptom score. There have been no large-scale randomised trials of HIFU. The results of the non-controlled studies are shown in Table 16 (*see* opposite).

Microwave therapy (*see* Table 17 (p. 122) and Table 18 (p. 123)[141–161])

The results of these treatments need to be stratified according to the type of energy used. Early treatments heated the prostate to about 42–46°C and were known as hyperthermia. The energy was applied per rectum or per urethra. Though there were some symptomatic improvements no objective evidence of destruction of prostatic tissue could be confirmed.[82]

Microwave hyperthermia

Transurethral microwave thermotherapy (TUMT) involves an ultrasound generator and receiver which converts the energy into heat, which is focused in the centre of the prostate lobes. The amount of energy determines the degree of heating. Hyperthermia results in very little tissue damage as measured by changes in serum PSA. No prostate tissue is removed for pathological diagnosis.

Conclusions on thermotherapy

The majority of studies report that this treatment is well tolerated by patients, but some indicate that temporary retention occurs in 25% of men following TUMT. Symptomatic improvement is found in all studies. Most studies have also found increased maximum flow rates or reduced residual urine. There is concern about the long-term effectiveness of the therapy, with some authors finding increasing failure over time, but others reporting a stable 60% success rate at two years. Hyperthermia is going out of fashion because of poor results. We are still awaiting the results of large-scale randomised trials incorporating acceptability, costs and long-term follow-up (*see* Table 18).

Table 15: Results for non-controlled trials of stents.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Guazzoni[130]									
I	91	69.3	12	14.1	6.4	55	9.3	15.7	69
II	44	73.1	12		4.5			13.1	
Kaplan[131]									
I	144	73.5	24	16.3	6.21	62	4.95	12.04	143
Milroy[132]									
I	54	75.7	6	17.9	5.2	71	9.9	19.41	96
II					8.3			16.61	
Oesterling[133]									
I	126	68	24	14.3	5.4	62	9.1	13.1	44
II					4.1			11.4	
Vincente[134]	22	80.3	12					66% in 6–4 ml/s 33% in < 6 ml/s	
Williams[135]									
I	96	(52–95)	12	17.94	3.36 (Madsen Iversen)	81	8	18.1	126
II					1.53		15		
Yachia[136]	65		16						

I = non-retention; II = retention.

Table 16: Results for non-controlled trials of high-intensity focused ultrasound (HIFU).

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Narayan[137]	42	68	6	24	7.8	68	8.8	20	127
Madersbacher[138]	50	67	12	24.5	10.8	56	8.9	13.1	47
Nakamura[139]	37	67.2	3	23.6	10.5	56	7.6	9.3	22
Uchida[140]	28	71.4	6	5.2 (IPSS)	2.8	46	8.8	10.8	28

Table 17: Results for trials of hyperthermia.

Trial	Number	Age (years)	Length of follow-up (months)	Symptom score	Post-treatment symptom score	Change in symptom score (%)	Flow rate (pre-operative)	Flow rate (post-operative)	Change in flow rate (%)
Abbou[141]									
Hyperthermia (TU)	66	65	12	10.9 (Madsen)		50	10.4		14
Sham	31	66		12.8		17	9.9		17
Hyperthermia (PR)	65	66		11.7		25	9.8		8
Sham	38	66		12.1		39	9		16
Kaplan[144]									
Hyperthermia	21	60.6	6.7	16.4	6.5	60	5.9	13.2	124
Montorsi[145]									
Hyperthermia < 70 years (5 sessions)	158	61	24	18.2 (Boyarski)	13.8	24	9.2	10.4	13
Hyperthermia > 70 years (0 sessions)	98	75	24				8.8	9.2	4.5
Retention	64	71	24		12		ng	12.1	
Bdesha[143]									
Hyperthermia	22	63.7	3	30 (WHO)	11.7	61	12.3	14.6	19
Sham	18	63.7	3	31	26	16	10.8	9.8	−9
Petrovich[146]									
Hyperthermia	63	66	12				8.3	11.91	43
Venn[142]									
TUMT	47	70.5	6	12.7		42			
Stawawtz[147]									
PR	22	63	19						
Sapozink[148]	21	67	12.5				11	15.9	
Richter[149]	37	70.5	11				3.4	9	

TU = transurethral; PR = per rectal.

Table 18: Results for trials of microwave thermotherapy.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Blute[155]	150		12	13.7	5.4	61	8.5	11.3	33
de la Rosette[157]	75		6	14.15	5.31	62	8.75	12.32	41
de la Rosette[157] (high energy)	105	66.6	6	13.6	5.5	60	9.6	14.1	47
de la Rosette[158] (high energy)	120	67	6	13.9	5.3	62	9.4	14.1	50
Eliasson[159]	172	68	12	12.7	6.6	48	9.8	10.9	11
Höfner[160]	140	69	40	13 (Madsen)				11.5	
Porru[161]	44	69	12	11.61 (Boyarsky)	3.04	74	8.29	12.78	54
de la Rosette[88]									
TUMT	25	64.1	3	13.2 (Madsen)	5.9	55	9.6	14	46
Sham	25	62.7	3	21.1 (Madsen)	8.2	61	9.7	9.5	−2
de Wildt[152]									
TUMT	47	66.3	12	13.7 (Madsen)	8.2	64	9.2	13.4	46
Sham	46	63.9		12.9	4.2	67	9.6	10.5	9.4
de la Rosette[150] (2-year follow-up)	301			14.1 (Madsen)	5		9.7	13.8	42
d'Ancona[153]									
TUMT	31	69	12	13.3 (Madsen)	4.2	68	10	16.9	69
TURP	21	69	12	13.8	2.8	80	9.3	18.6	100

Laser therapy (*see* Tables 19 and 20 (opposite) and Table 21 (p. 126)[162–191])

Transurethral visual laser ablation of the prostate (VLAP) or endoscopic laser ablation of the prostate (ELAP)

With contact ablation, a lower laser energy is applied, which heats up the tissue enough to cause it to necrose and slough with time. Compared to standard transurethral resection or TURP, the advantages of laser procedures are no significant bleeding, shorter hospitalisation and reduced operating time. On the other hand, there is a large amount of swelling in the prostatic urethra for 3–10 days, which requires temporary catheter drainage. In addition, patients can experience a few weeks of urinary frequency and irritation while the prostatic channel is healing. Its significant advantages are no bleeding and a short hospital stay.

One concern is that no prostate tissue is removed. Therefore, one cannot be certain that cancer does not exist. However, PSA and ultrasound-guided biopsy carried out before VLAP can minimise the risk.

Interstitial laser coagulation of the prostate (ILC[171–172])

This is similar to transurethral needle ablation of the prostate. A thin laser fibre is inserted into the prostatic adenoma via a transurethral or transrectal route under ultrasound or visual guidance. Laser energy is then utilised to induce local tissue destruction by heating. Preliminary data on small series of patients suggest it has potential as a viable minimally invasive surgical alternative for the treatment of BPH.

There are no large-scale studies of ILC. In one study, 20 men were treated with the indigo machine.[172] Flow rates increased from 7.9 ml/s to 13 ml/s and symptom scores decreased from 22.6 to 14.3 at six months. Another study[174] assessed 28 men. Flow rates increased from 6.7 ml/s to 16.2 ml/s and symptom scores decreased (pre-operative range was 19–26; post-operative range was 10–16).

Holmium laser treatment[173–174]

There are no large-scale randomised trials against TURP, but this is the procedure that most closely resembles the standard operation because large amounts of tissue are removed. It can be a time-consuming procedure.

TULIP (transurethral ultrasound-guided laser-induced prostatectomy) (see *Tables 22 and 23 on p. 127)*

In general, laser treatments have been shown to be effective, but associated with fewer serious side-effects compared with TURP. However, they are not quite as effective as conventional treatments and the duration of effectiveness is open to doubt. Finally, in the short term after treatment men suffer quite severe side-effects of dysuria and frequency, which have not been well documented.

Transurethral incision of the prostate (TUIP) (*see* Table 24 (p. 127) and Table 25 (p. 128)[192–199])

Previous studies have shown that this operation is nearly as effective as TURP and may be associated with fewer side-effects, such as retrograde ejaculation. However, large-scale studies with long-term outcomes have not been done. In addition, the procedure is best suited to small glands, which means that it might apply to only about 30% of men undergoing treatment. At present it is perhaps an underutilised procedure, but systematic reviews have brought this out. However, the number of men included in the trials is relatively small and the procedure has not become more widely adopted.

Table 19: Results of non-controlled trials of laser prostatectomy.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom scores (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Costello[175]	69	66.08	12		18.85	8	8.86	16.82	89
Cummings[176]	25		3		11.4	7	6.1	14.5	137
de Wildt[177]	40	63.8	6	21.7	6.3	71	8	17.1	114
Furuya[178]	66	72.6	12	18.5	4.8	74	6.4	10.4	63
Muschter[184]*	239	67.8	12	25.4	6.2	76	7.7	17.6	128
Narayan[179]	61	71.6	12	27.5	8	71	9.3	24.6	164
Narayan[179]									
(I)	41	70.4	6	23.2	8.6	63	8.5	18.4	116
(II)	39	73.9	6	24.9	7.2	71	9.1	16.6	82
(III)	20	67.9	6	23.2	7	70	8.6	17.8	107
Te Slaa[181]	105		6	21.3 (IPSS)	5.3	75	7.9	17	115
Te Slaa[182]	233	66.3	12	21.1 (IPSS)	3.6	83	7.5	16.3	117
Tubaro[183]	100		6	14.8 (Madsen)	5.45	63	8.59	11.6	35

*Also reported in de la Rosette *et al.*[88]
I = prostate volume < 40 ml; II = prostate volume 41–80 ml; III = prostate volume > 80 ml.

Table 20: Results of non-controlled trials of visual laser ablation of the prostate.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Kablin[185]	227	70	24	20.3	8.6	58	7.3	18.3	151
Kablin[186]	50	68	12	20.8	8.4	60	7.6	18.7	146
Malek[187]	47	69.6	5	22	10	55	9.5	15.7	65

Table 21: Results for controlled trials of laser prostatectomy vs. TURP.

Trial	Number	Mean age (years)	Follow-up (months)	Symptom score (before)	Symptom score (after)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Anson[162]									
ELAP	76	67.9	12	18.1	7.7	57	9.6	15.4	60
TURP	75	68.3		18.2	5.1	72	10	21.8	118
Costello[163]	34	67.9	6		9.27			15.75	
Laser									
TURP	37	68.2			4.43			19.1	
Cowles[165]									
VLAP	56	65.8	12	18.7	9.7	48	8.9	13.9	56
TURP	59	67		20.8	7.5	64	9.5	16.5	74
de la Rosette[188]									
Ultraline	44	65	12	32 (IPSS)	6.6	69	7.8	19.7	153
Urolase	49	64.6		21	1.7	92	7.9	12.7	61
Kabalin[168]									
Urolase	13	65	6	20.9	4.6	78	8.5	20.5	141
TURP	12	69		18.8	5.7	70	9	22.9	154
Kabalin[186]									
Urolase	13	67	12	20.9	4.3	79	8.5	21.6	154
EALP	12			18.8	6.3	66	9	21.6	140
Keoghane[167]									
Laser (contact)	76	69	3	19.9	9.6	52	11.8	21.3	81
TURP	72	70		19.4	6.5	66	11.4	21.8	91
Orihuela[189]									
Low-power laser	15	66	12	27.3	*c.* 4	66	5	*c.* 17	
High-power laser	14	59		26.1	*c.* 3		4.5	*c.* 20	
Uchida[166]									
VLAP (urolase)	50	71	12	22	7.6	65	9.1	16.4	80
TURP	50	66.7		21.1	3.5	83	8.5	21.6	154

Table 22: Results for non-controlled trials of transurethral ultrasound-guided laser-induced prostatectomy.

Trial	Number	Mean age (years)	Follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Schulze[190]	89	67	12	17 (Boyarsky)	5		7	15	

Table 23: Results for non-controlled trials of transurethral ultrasound-guided laser-induced prostatectomy.

Trial	Number	Mean age (years)	Follow-up (months)	Symptom score (before)	Symptom score (after)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Schulze[191]									
TULIP	20	64.5	12	19	*c.* 1		3.2	*c.* 15	
TURP	21	65.9		17.7	*c.* 3		2.4	*c.* 17	

Table 24: Results for non-controlled trials of transurethral incision of the prostate (TUIP).

Trial	Number	Mean age (years)	Follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Sirls[193]	41	63.4	12	12.5	6.9		10.3	15.3	

Table 25: Results for controlled trials of transurethral incision of the prostate (TUIP) vs. TURP.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Christensen[194]									
TUIP	35	63	36	16	8	50	7.8	10.9	40
TURP	38	62		16	4	75	9.7	14.6	51
Dorflinger[195]									
TUIP	17	67	3	15	2.5	83	10	15	50
TURP	21	71		17	1	94	9	19	111
Dorflinger[196]									
TUIP	22	69	3	14.5	2.5	83	10	8	−20
TURP	29	71		16	1	94	8	18.8	135
Larsen[197]	19	63	3	17	2	88	7.4	14.4	95
TUIP	19	63	3	17	2	88	7.4	14.4	95
TURP	18	61		17	2	88	8.6	16.3	90
Riehmann[198]									
TUIP	61	65	72	*c.* 15	*c.* 9		*c.* 11	*c.* 12	
TURP	56	64		*c.* 15	*c.* 10		*c.* 10	*c.* 19	
Soonawalla[199]	110	62.2	12						
TUIP	110	62.2	12			(96% satisfied)	3.82	11.21	
TURP	110	65.03				(90% satisfied)	3.99	10.91	
Sham	46	68		13		20			

Table 26: Results for non-controlled trials of electrovaporisation of the prostate.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Issa[201]	LP								
Narayan[202]	42	68	6 months	24 (IPSS)	7.8	67.5%	8.8	20	135.2
Kaplan[203]	25	67.4	3 months	17.8	4.2		7.4	15.3	

Transurethral electrovaporisation of the prostate (TVP) (*see* Table 26 (p. 128) and Table 27 (p. 130)[200])

Compared to the standard TURP, this procedure results in less bleeding, shorter hospitalisation and catheter times, and faster recovery period.

The procedure allows the grooved roller-ball electrode to rapidly heat the tissue to turn it into steam, leaving a space where the prostate tissue was previously present. The majority of heat is dispersed by a constant flow of water. The defect does not bleed because it is coagulated and sealed by the roller-ball electrode. However, large veins may still bleed and reports of late rebleeding following separation of slough have appeared. Technically, this is a new way to do a TURP and it can also be utilised to perform a TUIP.

Long-term data on its efficacy are not yet available, but multi-centre trials are under way to compare it to other procedures such as standard TURP. The major potential advantages of TVP compared to the conventional TURP and laser-assisted prostatectomy are lower cost, fewer side-effects, more rapid convalescence time and short hospital stay (overnight), as well as the simplicity of the procedure. This makes TVP a useful, safe and versatile tool in the treatment of the enlarged prostate disease that causes urinary outflow obstruction or BPH. Potential side-effects include delayed bleeding caused by separation of slough and an increased rate of later reoperation. Considerable energy is absorbed by the prostate and we do not know the optimum size of the prostate that can be treated by this technique.

Transurethral needle ablation of the prostate (TUNA) (*see* Table 28 (p. 130)[200–206])

Preliminary data on small series of patients suggest that this has the potential to be a viable, minimally invasive surgical alternative for the treatment of BPH. The amount of tissue destruction is likely to be small and to limit the size of gland treated by this technique.

One large-scale randomised trial was found in abstract form.[153] Over 50 men were randomised to the two treatments and followed up for over a year. Flow rates and symptom scores improved in both groups, but were better following TURP. On the other hand, fewer men developed complications after TUNA.

Minimal TURP vs. standard TURP[207]

This procedure is effectively an incomplete TURP and is meant to be a lesser procedure than standard TURP with fewer side-effects. The rationale appears dubious, and it is not recommended without further evaluation.

Economic evaluation of LUTS and BPE

The aim of economic evaluation is to compare alternative uses of resources. This is done by relating the benefits which result from one particular activity to the associated costs in terms of real resource use. It is then possible to detect projects with the maximum net present value or greatest cost-effectiveness (depending on the type of evaluation).

Any economic evaluation of health care should involve the comparison of at least two alternatives. Cost studies that do not involve comparisons of competing alternatives are merely descriptions of the costs of a procedure rather than evaluations. These are sometimes called cost-of-illness studies. The simple description of costs cannot support policy recommendations, as no indication is given of the benefits of one project relative to another.

Research reports concerning prostatectomy often mention the costs associated with the procedure, at least briefly. A number of these studies are not particularly helpful in that they only make assertions, e.g. that the yearly cost of surgery and hospitalisation for LUTS and BPE in the USA is in excess of

Table 27: Results for controlled trials of electrovaporisation of the prostate vs. TURP.

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Patel[200]									
TURP	21			22.5	5.3	76	8.2	18.2	122
EVAP	17			22.4	4.1	82	7.3	18.9	159
Kaplan[203]									
EVAP	29		3	15.3	5.3	65	8.2	14.9	82
LAP	29			14.7	7.6	48	9.7	13.7	41

Table 28: Results of trials of transurethral needle ablation of the prostate (TUNA).

Trial	Number	Mean age (years)	Length of follow-up (months)	Symptom score (baseline)	Symptom score (after follow-up)	Improvement in symptom score (%)	PFR (before)	PFR (after)	Improvement in PFR (%)
Bruskewitz[205]									
TURP	56	66	12	24.1	7.9	67	8.9	21	136
TUNA	65			23.9	11.7	51	8.9	14.6	64
Issa[201]	12		6	25.6	9.8	62	7.8	13.5	72
Schulman[204]	20		3	21.9 (IPSS)	10.2	53	9.5	14.7	55
Schulman[206]	48		36	21.6	8.5	61	9.9	16.9	71

US$1 million,[12] or that prostatectomy costs more than US$1 billion per year in the USA, or that the cost of managing LUTS is large in the UK.[35] Such pronouncements do not generally assist the policy decisions that must be made regarding prostatectomy.

Cost-of-illness studies

While these studies are not forms of economic evaluation, it is helpful to consider the costs obtained by such work. One study considered the cost of prostatectomy given various rates of operation based on variations both within and between countries. It was found that the dollar expenditure in the USA on TURP could vary between US$366 million and US$1195 million, depending on whether there was a low or high rate of operation (1975 prices).

Cost analyses/cost-minimisation analyses/cost-effectiveness analyses

There are a number of types of economic evaluation that can be pursued. In a cost analysis it is assumed that the outcomes of alternative policies are identical in order that the costs of the alternatives can be compared. A cost-minimisation analysis (CMA) is similar, though it is a full economic evaluation as there is some evidence on which to believe that outcome differences of the alternatives are non-existent or unimportant.[208] A cost-effectiveness analysis (CEA) compares the cost of an intervention with its benefits in terms of one outcome measure, e.g. increase in life expectancy or increase in continence or reduction in sexual functioning. It is not possible to compare more than one outcome measure with costs and obtain an unambiguous answer unless all indicators move in one direction or unless the outcomes can be combined in index form, as in a cost-utility analysis (CUA).

A CMA by Meyhoff compares the costs of TURP and open prostatectomy,[214] having previously carried out a randomised trial which found few differences between the clinical outcomes of the two operations for those with medium-sized prostates (25–75 g). Clinical outcomes considered included symptom relief, sexual functioning and long-term results. The economic evaluation was from the societal viewpoint, and both direct and indirect costs were included. The estimated average cost for one patient undergoing TURP was US$4071, and for open prostatectomy was US$7534 (1983 prices). It was therefore concluded that TURP was more cost-effective than open prostatectomy for medium-sized BPE.

Other clinical trials[93] and observational studies[116] have concluded that TURP has a significantly shorter length of stay than open prostatectomy and that at least from the point of view of the hospital it is likely to be more cost-effective.

An economic evaluation was also carried out concerning the cost-effectiveness of uroflowmetry as a means of screening patients for prostate problems.[209] Instrumental measurements of peak flow conducted in the hospital were compared with a simple method of timed urine flow measurement performed at home by the patient. It was concluded that this was a valid method of revealing a weak stream, and therefore the possibility of prostate problems. A broad estimation of costs from the hospital viewpoint led to the conclusion that, as the home method was free, it was more cost-effective.

Cost-utility analyses

A particular form of the cost-effectiveness study is the cost-utility analysis (CUA). In the CUA, as in the CEA, there is only one measure of outcome. In a CUA this is usually the quality-adjusted life-year (QALY), a measure of utility in the form of life expectancy weighted for quality of life. The QALY is in its infancy as a practical outcome measure and still has many associated problems. Several studies have considered utility measures in conjunction with prostatectomy. However, none has combined patients' utility measures of outcome with equivalent costs.

In 1983 a paper was published by Woodward *et al.* that combines two indices regarding prostatic disease to form the Prostatic Health Status Index (PHSI).[210] Although the authors state that transformations should be based on utility functions, the authors' clinical evaluations are used to demonstrate the index. The PHSI is combined with data from the nine years of the project to form QALYs, and with cost data, although it is not made explicit where these cost data come from or what they represent. The index is then used to show the effects of discounting on whichever of the alternatives, open or TURP, is eventually chosen. As the QALY data are based on the authors' clinical evaluations and the cost data are unexplained, it is inappropriate to use the results to recommend particular policies. The authors show that, given different assumptions and with different discount rates, it is possible to present either policy as preferable.

Research has been furthered by the formation of quality-adjusted life-months (QALMs).[211] The authors combine data on patient preferences and Medicare claims data with the utilities estimated by Woodward *et al.* to compare immediate transurethral resection of the prostate with a do-nothing alternative, referred to as 'watchful waiting'. QALMs are compared for a number of alternatives, but for the base-case analysis of a 70-year-old, sexually active, continent man it was discovered that immediate surgery resulted in the loss of 1.01 months of life expectancy compared with 'watchful waiting', but taking quality of life into account, there was a gain of 2.94 QALMs.

The figures for QALMs are, of course, heavily dependent on the probabilities and utilities assigned to various outcomes. Operative mortality was found to be the single most influential probability affecting the QALMs, while some evidence was given that the baseline utility for men with moderate symptomatic prostatism was too low. Without accurate assessment of risks, and utilities based on societies' preferences, the QALM (or QALY) is unlikely to be helpful in making policy decisions. In addition, the utility data must be combined with cost data for a full economic evaluation. Despite this, the analysis is useful in that it compares many different alternatives, with the aim of identifying those particular patients for whom a TURP is most beneficial. It therefore goes some way towards answering fundamental questions regarding which diseases and what level of severity of disease should receive priority in treatment.

The time trade-off approach has been used to elicit utility values for surgical and non-surgical management from 20 men with LUTS.[212] The values obtained in this way were generally higher than those of Woodward *et al.* For example, the value obtained by time trade-off for a state of incontinence was 0.8, while that of Woodward *et al.* was only 0.5. Although the utility values in this study were not incorporated into QALY outcome measures and the sample size was very small, it was shown that such a methodology was a feasible means of eliciting patients' utility scores for prostatectomy and the effects of LUTS.

Cost–benefit analyses

An alternative to the CUA is the cost–benefit analysis (CBA), in which the benefits of an intervention are valued in monetary terms so that they can be directly compared with the costs. This is the only type of economic evaluation that can indicate whether it is intrinsically worthwhile carrying out an intervention, rather than just whether one intervention is relatively more beneficial than another for equal costs. The problems associated with the valuation of the essentially intangible benefits of interventions in the area of health care are inevitably large, and such evaluations often generate much criticism. Perhaps for this reason, no CBAs have been found concerning prostatectomy.

Conclusion

There has been only one study[213] performed which takes into consideration both the costs and outcomes of prostatic surgery. This concluded that for medium-sized prostates a TURP was more cost-effective than open prostatectomy. However, the formation of utility measures, if combined with cost data, could potentially be of great value in informing policy on elective surgery for LUTS and BPE.

Ideally, research should be implemented which considers both the relative costs and benefits of prostatectomy for varying severity of LUTS, and the relative costs and benefits of prostatectomy for BPE compared with the relative costs and benefits of other elective surgery. Only when this is done will it be possible to establish priorities in treatment.

7 Recommendations and models of care

In considering purchasing decisions, it is necessary to distinguish between those patients with acute and chronic urinary retention who require emergency catheterisation and prostatectomy, and those who elect for a prostatectomy because of bothersome urinary symptoms. Clearly, all patients with acute urinary retention will require emergency catheterisation, but there is some uncertainty over whether patients should progress immediately from catheterisation to a prostatectomy or to a 'trial of voiding' before deciding on the necessity for a prostatectomy. Currently, practice differs among urologists.[40]

In men who only have symptoms, the risk of progression to retention if they are not offered TURP has been shown in an overview of men entered into a trial of finasteride. Following drug treatment, the rates of elective prostatectomy were 4.2% in men treated with finasteride compared with 6.5% in men treated with placebo, and the rates of urinary retention were 1.1% in men treated with finasteride compared with 2.7% in men treated with placebo.[214] The number of men prevented from developing complications by medical treatment is, however, relatively small[215] and it would not be cost-effective to offer medical treatment to all men with symptoms solely on the grounds of preventing complications in the very few.

The largest group of patients receiving prostatectomy are those electing for the operation because of bothersome urinary symptoms (approximately 65%). The uncertainty and debate surrounding the diagnosis and treatment of LUTS, and the lack of consensus about who should have treatment and at what stage in the development of the disease means, however, that purchasers have very limited information on which to base their decisions. To place too much stress on a refined analysis of the status quo would be quite inappropriate in the face of accumulating research evidence that calls into question any certainties concerning appropriate criteria for treatment. That prostatectomy is an effective intervention in some cases is not in doubt. There is considerable doubt, however, concerning the circumstances in which it is effective, and which procedure is preferable in certain cases. It should also be noted that provision of prostatectomy in England and Wales is currently low by international standards.

Conventional model

In this current model, GPs see men with symptoms or complications of BPH as they present. A GP will expect to see 50 men per year per 1000 men aged over 60 (equivalent to 10 000 of the general population). Twenty will be referred on, 20 may be reassured, 10 will have operative treatment and 10 will be treated by drug therapy. The standard mode of operative management will be by means of TURP or TUIP. Total costs will be £40 000 per year for a group of 1000 men aged over 60 years, but as pointed out earlier, the true in-hospital costs of the provision of this service are likely to be much greater than this. Increased information about prostate diseases among men in the community is likely to increase the number of men presenting to GPs. Our recommendations are that men with mild to moderate symptoms and no evidence of prostate cancer or impaired bladder emptying can be safely managed by 'watchful waiting'. Men who do not respond to this management may be treated by drugs (α-adrenergic blockers or finasteride) or referred to a local urologist.

Increased local management

It may be that by the provision of easy-access prostate assessment clinics and the use of specially trained nurses provided with flow meters, more men might be managed locally, and only those with severe symptoms or complications would be referred on to hospitals. This may be more costly – particularly because more men would be likely to be managed with drug treatment, which costs in the order of £300 per year. A more ready policy of treatment of such men by means of drugs might at first sight be likely to result in decreased demand for surgery. However, there are likely to be more subtle changes. First, in the UK, men are offered treatment only when they have severe symptoms and side-effects and a reduced demand for surgery may not be seen. Second, the pool of treated men may well increase significantly, increasing global costs without decreasing the numbers referred for surgery. Another cost is the requirement to maintain and check up on the accuracy of flow meters and ultrasound scanners.

The numbers of men presenting to a GP per year may not justify the costs of specially trained nurses and it may be more cost-effective to arrange nurse-led clinics to be held and supervised by urologists in secondary care. The other option is for primary care trusts (PCTs) to set up prostate assessment clinics, but the comments about quality control are important.

New technology

More men are being managed by means of new techniques, such as stents, microwaves and lasers. While these treatments may be less prone to side-effects, they may turn out to be more costly and less cost-effective in the long term. It is our view that purchasers should be asking providers for details of when men are treated with new technology because we consider that, in general, such treatments should be provided only in the context of large randomised trials.

Conclusions

The current provision of TURP in England and Wales of about 40 000 to 45 000 operations per year is low compared to international standards. There are no data suggesting that this number is incorrect or unsafe. The proportion of men with chronic retention and acute retention compared to the whole is relatively large, suggesting that UK urologists are relatively conservative. Guidelines produced by the Royal College of Surgeons and British Association of Urological Surgeons are likely to iron out some of the differences among urologists for threshold for intervention in men with symptoms.

Men with LUTS and BPE are not more prone to develop prostate cancer compared with the rest of the population. However, prostate cancer can present with lower urinary tract symptoms, and exclusion of locally advanced prostate cancer is important.

There is no indication for setting up routine screening for early prostate cancer. Initial assessment should be carried out by the GP. Nurse-led prostate assessment clinics staffed by specially trained nurses and overseen by a consultant or committed, interested GP might in the future offer an intermediate form of assessment which might make urology outpatient visits more effective. If GPs are going to manage men with LUTS in primary care by means of drug treatment, they should be confident in their own technique of rectal examination so that they can exclude locally advanced prostate cancer, which can also be a cause of symptoms. Access to a general urology clinic should also be available. Between 150 and 250 per 100 000 men aged over 60 have significant symptoms in the community.

The evidence suggests that men with mild or moderate symptoms without evidence of complications or prostate cancer can be managed by ‘watchful waiting’. The evidence also suggests that α-adrenergic blockers and finasteride are more effective than placebo treatments and that, in some trials, finasteride is less effective than α-adrenergic blockers. Long-term data have shown that men who have responded to finasteride in the short term and who are kept on long-term treatment have fewer admissions with acute retention or for prostatectomy. However, the number of operations prevented is relatively low. Long-term drug treatment may be provided in primary care.

Men seen in outpatient clinics should undergo clinical history taking and examination. Renal function should be assessed, and urinary infection and diabetes should be excluded. There is no need for routine IVU or upper tract imaging, but flow rates should be measured and urodynamic studies should be available for selected patients.

Men with acute retention require urgent catheterisation and either urgent admission or urgent assessment by the urologist. Men with chronic retention require urgent outpatient assessment; those with renal impairment need urgent admission. Men with severe symptoms or problems should be referred to a urologist.

8 Outcome measures, audit information and research needs

This chapter has drawn attention to the paucity of evidence that may support an informed judgement as to the health care requirements for treatment for LUTS and BPE.

In particular, it should be noted that there are no good data on:

- true costs of new treatments
- cost-effectiveness of new treatments and new technologies
- long-term outcome for new treatments.

Information

Hospital data can never permit an assessment of the natural history of LUTS and BPE, the requirement for treatment, or the outcome or effectiveness of treatments, because of the large number of men who are not referred.

Increasing management of men in primary care should be monitored, as should the use of potentially expensive medications.

Audit

Large-scale audits of TURP have now been carried out in England and have shown good levels of performance in keeping with international standards. The costs of such complex audits are considerable. It may be that PCTs will want urologists to demonstrate participation in audit programmes. Monitoring of complications and feedback of untoward incidents would be a good initial step, rather than insisting on more precise measurements which might carry considerable costs.

Possible measures of quality might include:

- management of acute retention – if men are discharged home with a catheter, how soon are they readmitted for elective surgery (excluding those who are waiting for intercurrent illness to improve)?
- return to theatre rates
- late reoperation rates
- proper treatment of intercurrent urinary infection.

Death rates are not a good measurement because they are so low, even in men with retention or prostate cancer.

In primary care, it may be that demonstration of appropriate 'watchful-waiting' periods before referral to secondary care might be a good measurement. Ensuring that men with severe symptoms or impaired bladder emptying are referred to secondary care might be another measurement.

Research

There are weak relationships among BPH, BPE, BOO, LUTS, clinical findings, autopsy evidence and objective measures of urinary function (e.g. urodynamic studies). Prostatectomy is the current standard treatment for BOO caused by BPE, but there is uncertainty about how to distinguish obstruction from other problems of the urinary tract. There is also debate about which type of prostatectomy is the most effective (open or transurethral), and whether or not alternative therapies (drug and new technology) might be more appropriate in some cases.

There is a need for population-based data to build up a greater understanding of the natural history of LUTS and BPE, to investigate patient perceptions of the disease and its treatments, and to assess the outcomes of patients choosing drug treatments and/or surgical procedures compared with those preferring more conservative treatments, including 'watchful waiting' and no treatment. There is also clearly a need for outcomes research, which draws on existing data (mortality and readmission rates, length of hospital stay, use of medication), and dedicated enquiries (measures of perceived health, including activities of daily living, patient satisfaction and well-being, perceived levels of change in life and state of health, as well as specific post-operative complications).

There is a need for research into the following areas:

- comparison of drug treatments and 'watchful waiting' in primary care
- comparison of drug treatment in primary care and the use of new technology as a single treatment
- long-term data on the randomised trials that have been funded by NHS R&D to compare new technologies with conventional treatment
- provision of care and assessment by GPs with a more conventional approach
- basic science studies of prostate growth
- basic science studies of the pathophysiology of the ageing prostate and bladder.

Appendix 1

New treatments used in the management of men with LUTS and BPE

Balloon dilatation

At the time of our review there were three major balloon designs: Optilume, Dowd-II and ASI Uroplasty. Balloon dilatation is a technique that has become part of urological practice without evaluation of its effectiveness and cost-effectiveness.

A number of small, observational studies have been undertaken.[120–121] These studies reported mixed results. A success rate, in terms of symptomatic and maximum flow rate improvement, was reported in 46–66% of patients, but in other studies the success rate was lower (one patient out of 28). Most studies reported that the procedure was best for small glands, and resulted in low levels of complications, including retrograde ejaculation. One study reported poor results using the technique in patients with acute urinary retention, with only three of 19 patients able to void following the treatment.

Lepor *et al.*[120]

Lepor *et al.*[120] randomised 31 symptomatic men to either balloon dilatation or cystoscopy. Both groups reported statistically significant improvement in symptoms, as measured on the Boyarsky schedule, but there was no statistical difference between the two groups. Changes in maximum flow rates were not significantly different from baseline in either group.

Chiou *et al.*[121]

This paper has been included for analysis because it has a treatment control group. However, it did not meet the required minimum number of patients and did not state whether baseline parameters for the two groups were similar. Balloon dilatation was compared to TUIP. Symptomatic assessment was measured by the Madsen–Iverson score and dilatation involved the use of the sized-to-fit Uroplasty balloon (Advanced Surgical Intervention, California, USA); TUIP was as described by Orandi.[123] Good responses were defined by an improvement in symptom scores of 50% or more.

The results demonstrated a mean increase in peak flow of 54% in the balloon dilatation group ($n = 16$) vs. an improvement of 101% in the TUIP group ($n = 14$). Side-effects were mild and short-lived for balloon dilatation. In the TUIP group one patient (7%) had delayed bleeding and clot retention, while three (21%) developed a urethral stricture, although these were mild and responded to treatment. Success rates in terms of symptom scores were 87% (dilatation) and 86% (TUIP). Marked improvements were seen in 56% and 71%, respectively. The method of randomisation was not reported. Moreover, after between 6 and 41 months of follow-up, 75% of the balloon dilatation patients had developed symptomatic recurrence compared to 20% of those treated by TUIP.

Donatucci *et al.*[124]

This was a randomised trial of balloon dilatation vs. TURP in 51 men. Balloon dilatation was performed using a 75-F double balloon dilatation system (Advanced Surgical Intervention, California, USA). Twenty-six patients were randomised to receive balloon dilatation and 25 to the TURP arm. The two groups had similar baseline measurements for all parameters. Symptom scores (using the Madsen scale) decreased from 14.1 to 7.3 over 18 months for balloon dilatation compared with a decrease from 13.6 to 7.7 for TURP. Uroflowometry showed an increase in peak flow (ml/s) from 11.8 to 16.1 for balloon dilatation compared with an increase of 12.2 to 19.8 for the TURP group. Complications reported for TURP included clot retention (8%), retrograde ejaculation (84%) and bladder neck contracture (4%). Only retrograde ejaculation was reported as a complication of balloon dilatation (7.7%).

Klein *et al.*[125]

This trial included only eight patients. However, it did include a control group and the patients were followed up for 24 months. Very little detail was reported. Of the five men undergoing dilatation, two had long-term improvements and at two years did not require any further intervention, although neither was voiding as well at this time as immediately post-operatively. Two patients had small improvements and sought surgical intervention for their continuing symptoms and one had no improvement. Of the three men in the observation group, two remained stable and one deteriorated. Only a single size balloon was used in this trial. Patients were randomly assigned either to receive treatment or for observation only.

Microwave treatments

Abbou *et al.*[141]

Two hundred male patients with LUTS were randomised to hyperthermia or placebo (i.e. a sham operation) in a single-centre trial. A second experimental group was randomised to receive hyperthermia via the transrectal route, and was also matched to a sham treatment group. Evaluation was carried out at 3, 6 and 12 months.

Both transurethral and transrectal hyperthermia treatment groups showed an improvement in peak flow rates (4% and 8%, respectively). However, the flow rates in the sham-treated men also improved and there was no significant improvement in objective response for hyperthermia treatment via the transrectal or transurethral routes in this trial. Symptom scores measured using the Madsen score improved by 50% and 25% for transurethral and transrectal routes, respectively. This was a statistically significant benefit for the transurethral route (17% improvement in the sham group), but not for the transrectal group (39% improvement in sham group).

Complications of both routes included urethral bleeding, pain and acute retention. These were found more frequently in men treated by the transrectal route, who also reported complications of rectal pain, faecal incontinence, chest pain, tachycardia and fainting. This route also resulted in more men withdrawing from treatment. No complications were reported for sham treatment.

Early complications of transurethral hyperthermia included urethral bleeding (27%), cystitis (18%), prostatitis and 6% unspecified other complications. Overall, 45% of patients who received treatment suffered from complications vs. 35% of the sham treatment group. In men treated via the transrectal route, 11% suffered from urethral bleeding vs. 13% in the sham group, 3% suffered from cystitis vs. 11% in the sham group, and 18% suffered from overall complications vs. 24% in the sham group. The study used three different devices for transrectal treatment (Prostathermer system, Biodan Medical Systems; Prostcare, Brucker Spectrospin; and Tecnomatix Medical, Belgium) and three devices for transurethral treatment (Theorem II, Technorex; Prostcare, Brucker Spectrospin; and BSD-50, Medical Corps, USA). The frequency of treatment was 1–3 hours and consisted of a single occasion for the transurethral route and six sessions over three weeks for the transrectal route.

Venn *et al.*[142]

In this controlled clinical trial, 96 patients were randomised to receive hyperthermia ($n = 48$) or sham treatment ($n = 48$). The method of randomisation was by selection of a sealed envelope. The baseline parameters of the two groups prior to operation were similar. Outcome was assessed subjectively, by AUA and Madsen symptom scores, AUA bothersome score and objectively by uroflowmetry.

The subjective evaluation demonstrated a decrease in symptom scores of around 40% in both groups. The only significant difference between the hyperthermia and sham treatment groups was the AUA bothersome score at 3 months, but this difference was not significant by 6 months. Objective parameters did not show any statistically significant difference between active and sham treatment.

Bdesha *et al.*[143]

This study did not fulfil the minimum requirement for trial size. However, it was carried out as a prospective randomised trial and included a control group. Residual urine volume decreased significantly in the control group vs. the group receiving sham treatment , but there was no difference in peak flow rates between the experimental and control groups. However, in terms of symptom score, taking into account frequency, nocturia, force of stream, hesitancy, terminal dribble, urgency, intermittency and incomplete voiding, there was a significant decrease in the active treatment arm vs. the control group ($p < 0.001$, $n = 22$ in treatment group and $n = 18$ in sham treatment group). The mean decrease in overall symptom scores was 63% in the thermotherapy group and 16% in the control group. No formal analysis of global outcome was reported. However, patients were asked for their opinion on the treatment they received. In the treatment group, 77% said they felt better, compared with 50% of the sham treatment group. Fifty per cent of those in the sham treatment group thought they had received active treatment, although the authors do not confirm whether these were the same patients who said they felt better; 86% of those receiving hyperthermia guessed correctly that they were in the treatment group. Complications of treatment were briefly reported, but did not include any severe mid- or post-treatment complications and all resolved within 48 hours of treatment.

The outcome was assessed at 3 months, and the trial was randomised by use of sealed envelopes. Patients had heat pads placed on their abdomens to minimise the suspicion of sham treatment. The treatment consisted of one single 90-minute session using a LEO (Laser Electro Optics) Microtherm with a variable power outlet and a maximum delivery of 20 W at 915 MHz.

Microwave thermotherapy

de la Rosette[88]

In this study patients were randomised to receive thermotherapy ($n = 25$) or a sham procedure ($n = 25$). The method of randomisation was not described. The delivery of the microwave therapy was carried out using the Prostatron device. However, no further details of the treatment were given in this article.

Parameters including average age and prostatic size were similar for the treatment and sham groups. Although both groups were followed up for one year, statistical analysis between the groups has only been made at 12 weeks as patients in both groups were offered active treatment after this time, minimising the usefulness of the study. There was a significant reduction in Madsen symptom scores in patients who received TUMT (13.2 to 5.9 at 12 weeks, falling further to 3.2 at 26 weeks). In the sham group, the reduction was markedly less, although symptom scores did record a drop from 12.1 to 8.2 at 12 weeks, rising to 9.1 after one year. At one year, 92% of those receiving TUMT and 38% of those in the sham operation group had a reduction in severity of symptoms of > 50%. Uroflowmetry showed a statistically significant improvement in those receiving TUMT, but not in the sham group. In patients who had been given sham treatment, repeat treatment with TUMT brought symptomatic and uroflowmetric improvement. However, in patients who had received TUMT and who had a second round of TUMT treatment, no further improvement was observed. Only four patients in the TUMT group, but more than half of those in the sham group, opted for a second treatment. There was no observed relationship between prostatic size and treatment effectiveness, by subjective or objective evaluation.

A study available in abstract form only[150] demonstrates that the benefits seen following TUMT appear to be persistent at 2–3 years, but start to decline at 4 years.

Roehrborn *et al.*[151]

This study, available in abstract form only, compared active and sham treatment with the Dornier machine in 205 men. AUA scores decreased in both groups (active, 23.7 to 12.1; sham, 23.8 to 17.5) and flow rates increased in both groups (active, 7.7 to 9.6 ml/s; sham, 8.1 to 9.1 ml/s), but active treatment was superior.

de Wildt *et al.*[152]

In this prospective, randomised controlled trial, 93 patients received TUMT ($n = 47$) or sham treatment ($n = 46$). The method of randomisation was not reported. There were no statistically significant differences between the baseline parameters of the two groups. Eighty-eight patients were available for assessment at 3 months and 63 patients at 1 year. Patients in the sham treatment group reported an early significant improvement in symptoms (Madsen scores decreased from 12.9 to 10.4), but peak flow rates did not improve in the sham group. Both active and sham treatments caused a sustained improvement in symptom scores and flow rates at 1 year. However, the improvement in patients who received TUMT was significantly better than in those receiving sham treatment. The only significant difference between the two groups after 1 year was in the post-void residual volume and the voided fraction, which favoured TUMT over sham treatment.

D'Ancona *et al.*[153]

This randomised study of TUMT vs. TURP was published in 1997. A total of 52 men were studied and outcomes were assessed at 12 months: 78% of men felt significantly improved after TURP compared with 68% after TUMT, and flow rates were improved by 100% and 69%, respectively. At 1 year, TURP provided slightly better results.

Dahlstrand and Pettersson[154]

A total of 71 men were randomised. Madsen scores decreased in both groups (TUMT, 12.1 to 3; TURP, 13.6 to 2) and flow rates increased (TUMT, 8.4 to 11.9 ml/s; TURP, 8.3 to 18.6 ml/s). Four men required TURP in the TUMT group. Five men required reoperation after TURP (three early operations for bleeding and two late ones for bladder neck stenosis). The results were maintained at 5 years, but flow rates were better after TURP.

Laser treatments

Anson *et al.*[162]

In this controlled trial, 151 patients were randomised to receive ELAP ($n = 76$) or TURP ($n = 75$). Patients were followed up for 1 year. The method of randomisation was by means of computer-generated randomised lists. The urolase right-angle laser fibre was the delivery system used to deliver 60 W energy from a Nd:YAG laser. Treatment was delivered at 2, 5, 7 and 10 o'clock positions and lasted 60 s at each point. The baseline characteristics of the two groups were similar. Of the initial patients enrolled to each group, nine withdrew from the ELAP group and five from the TURP group. Of the patients who had received ELAP, five had treatment failure resulting in further surgery (BNI or TURP). Of the remaining patients, 131 were available for follow-up at 1 year. Both groups reported statistically significant improvements in symptom scores (AUA) and peak flow rates. There were significant differences between the two groups with respect to symptom scores, which favoured TURP over ELAP. The scores for patients treated by TURP fell from pre-operative levels of 18.2 to 5.1, compared with patients treated by ELAP whose scores fell from an average of 18.1 to 7.7. TURP was also favoured over ELAP for objective outcomes such as flow rates, voided volumes and post-void residual urine volume.

The reported complications included dysuria in five patients who had received TURP (7%), and 25 patients following ELAP (33%). This decreased with time, but was still significantly higher in the ELAP group (15%) at 3 months than in the TURP group (1%).

One advantage of ELAP over TURP was the lack of haemorrhage requiring blood transfusion. None of the patients treated by ELAP required a transfusion, compared with 16% of patients treated by TURP.

Costello *et al.*[163]

In this randomised prospective trial, 34 patients were treated by laser prostatectomy and 37 were treated by TURP. The method of randomisation was by assigning alternate patients to different groups, which is not an ideal method. Both groups had similar baseline parameters for age and prostate volume. However, objective uroflowmetry and symptom scores for the groups prior to treatment are not reported. Fifty patients were followed up for evaluation at 6 months. The urolase right-angle laser fibre was the delivery system used to deliver 60 W energy from a Nd:YAG laser. Treatment was delivered at 2, 5, 7 and 10 o'clock positions and lasted 60 s at each point. No difference was found between the two groups when evaluated by maximum flow rates 6 months after treatment. However, evaluation by symptom scores demonstrated that they remained higher in patients who had been treated by laser prostatectomy (9.27) than in men treated by TURP (4.43). Mean flow rate for patients treated by laser was 16 ml/s, compared with 19.1ml/s in men treated by TURP. More serious complications were reported in the TURP group (22%, including three patients who required blood transfusions) compared with the laser group. However, 41% of the patients treated by laser therapy required treatment for dysuria, although these symptoms eventually resolved. Sexual potency and urinary continence were maintained in all sexually active patients post-operatively. However, while 87.5% of sexually active patients treated by laser maintained antegrade ejaculation, this was only preserved in 27% of those treated by TURP. It is assumed, although not specified, that treatment was ultimately successful for all of those treated by TURP, as no reoperations were recorded. In the group treated by laser, three patients (9%) underwent TURP during the 6-month follow-up period because of failure to improve. One of these patients underwent a second TURP and was reported as suffering from detrusor failure, and the other two patients are reported as having received inadequate laser energy for the size of prostate.

The authors of this study report that with equivalent lengths of hospital stay for both groups, there is a slight economic advantage of TURP compared with laser. However, they also report that if laser treatment can be carried out on an outpatient basis, as reported by Leach *et al.*,[164] then there is a significant economic advantage of laser treatment over TURP.

Cowles *et al.*[165]

A total of 115 men with symptomatic BPH were treated by TURP ($n = 59$) or VLAP ($n = 56$). The method of randomisation was a computer-generated chart, and the baseline characteristics of the patients (age, prostate volume, peak flow rate [PFR] and post-void residual urine [PVR]) were similar for both groups, with the exception of the AUA symptom score, which differed between the groups, VLAP patients having a mean symptom score of 18.7 compared with 20.8 for those patients in the TURP group. There was also a difference in the percentage of patients who had received previous treatment for BPH, which was higher for those randomised to receive TURP (28.8%) than those randomised to receive VLAP (16.1%). The urolase fibre was employed for delivery of the Nd:YAG laser energy (Trimedyne, CA, USA). In total, 40 W of power was directed at segments of the prostate for 60 s at the 3 and 9 o'clock positions, and for 30 s at the 12 and 6 o'clock positions. Patients were followed up for 12 months and evaluated by AUA symptom score, peak urine flow, post-void residual volume and quality of life. After follow-up for 1 year the clinical results for VLAP demonstrated a mean decrease in symptom scores of 9, compared with a mean decrease for TURP of 13.3. The peak flow rate increased in patients treated by TURP by 7 ml/s, compared with an increase of only 5.3 ml/s for patients treated by VLAP. TURP had a significantly longer procedure time (45.2 minutes) than VLAP (23.4 minutes) and also required a longer hospital stay (3.1 days) than VLAP (1.8 days). A significantly greater proportion of the group treated by TURP reported that their quality of life was improved 1 year post-operatively (93%) compared with those treated by VLAP (78.2%). The authors categorised complications as serious (i.e. impotence, infection, stricture, blood transfusion) or non-serious (i.e. retention, dysuria, hesitancy, dribbling). By these definitions, a significantly lower number of serious complications was suffered by VLAP patients (10.7%) than by TURP patients (35.6%). Patients treated by VLAP, however, had a considerably higher frequency of non-serious complications (51.8%) than those treated by TURP (28.8%).

Uchida *et al.*[166]

One hundred patients were enrolled in this non-randomised trial and treated by TURP ($n = 50$) or VLAP ($n = 50$). The urolase right-angle laser fibre (CR Bard, Covington, KY, USA) was used as the delivery system for Nd:YAG laser energy. Laser energy was delivered at 2 or 10 spots, 60 W per application, each for 60 s and the patients were followed up for 12 months. The effectiveness of the treatments was assessed by IPSS symptom scores, peak flow rates, post-void residual volume and estimated prostate volume. The clinical response was judged as excellent, good, fair, poor or worse. The baseline characteristics of the two groups were similar, with the exception of mean age, which was lower in the TURP group (66.7 years) than the VLAP group (71 years). This was a statistically significant difference, but the authors do not report how the patients were selected to receive TURP or VLAP. Therefore it is not clear whether younger patients were specifically selected to receive TURP or not. This may have some bearing on the overall outcomes. VLAP was a significantly shorter procedure than TURP (18.2 minutes, compared with 46.5 minutes for TURP), and resulted in a shorter hospital stay (8.3 days, compared with 13 days for TURP). However, the catheterisation time for VLAP (8.1 days) was significantly higher than that for TURP (3.5 days). The overall effectiveness at 12 months was measured by improvements in symptom scores, peak flow rates and PVR. International Prostate Symptom Score (IPSS) decreased from 22 to 7.6 for patients treated by VLAP, and from 21.1 to 3.5 for patients treated by TURP. Peak flow rates increased from 9.1 to 16.4 ml/s for VLAP and from 8.5 to 21.6ml/s for TURP. At 12 months, the overall clinical response after VLAP ($n = 29$) was judged to be excellent, good or fair in 93.1% of patients, compared to 100% of those treated by TURP ($n = 16$).

Keoghane *et al.*[167]

A total of 148 patients were enrolled into a double-blinded randomised trial to assess the effectiveness of laser ablation of the prostate (LAP; $n = 76$) compared with TURP ($n = 72$). The outcome was evaluated using uroflowmetry and AUA symptom scores. Patients were followed up for 3 months only. They were selected for treatment by the use of random-number tables in a 1:1 ratio, and treatment options were determined by sealed envelopes kept in the operating theatre. Laser-energy delivery was achieved using an Nd:YAG system (Surgical Laser Technologies, USA). The baseline characteristics of the two groups were not reported. The mean operating times for the two procedures were similar. However, the median blood loss suffered by patients treated by TURP was 200 ml, compared with 39 ml for patients treated by LAP. The median catheterisation time for LAP patients was 1 day (range 0–9) compared with 2 days for TURP patients (range 1–20), and the median number of nights in hospital was also lower for patients treated by LAP (3) than TURP (4). Mean symptom scores for patients treated by LAP were not significantly different from those for patients treated by TURP at 3-month follow-up. However, the frequency of complications reported for laser was lower than for TURP.

Kabalin *et al.*[168]

Twenty-five patients were entered into this comparative study of laser prostatectomy vs. TURP. The effectiveness of treatment was evaluated by AUA symptom scores and uroflowmetry. Laser energy was delivered by the urolase right-angle firing fibre. A standard Nd:YAG laser was used at 40 W power setting and energy was applied for 60 s to each lateral lobe at the 3 o'clock and 9 o'clock positions, and for 30 s at 6 o'clock and 12 o'clock. The trial was randomised but the method of randomisation was not reported. Patients were followed up for 18 months, by which time peak flow rates for laser therapy had increased by 135%, and for TURP by 136%. Symptom scores for patients treated by laser decreased from 20.9 to 6, and they decreased from 18.8 to 6.4 for patients treated by TURP. Only one patient in the TURP group reported a long-term complication (urethral stricture), and this was successfully treated. The early results of this trial were previously published, and included baseline characteristics of the two groups which showed a significant difference in the estimated size of the prostate. Short-term complications were reported and were more frequent in the TURP group (42%) than in the laser prostatectomy group (15%). Antegrade ejaculation was preserved in 100% of the patients treated by laser at 3 months, although one patient (8%) subsequently developed retrograde ejaculation. In the TURP group, 90% developed retrograde ejaculation.

Carter *et al.*[169]

A total of 204 men were randomised. Most patients were improved, but better results were found after TURP compared with laser in terms of symptom scores and quality of life in the first 2 months.

Tuhkanen *et al.*[170]

This study assessed 34 men. Laser treatment caused less bleeding than TURP (71 vs. 310 ml) and took longer (71 vs. 46 minutes). Catheter time was greater following laser treatment. TURP resulted in greater flow rates (TURP, 7.1 ml/s to 16 ml/s; laser, 8.7 ml/s to 13.9 ml/s) and reductions in symptom scores (TURP, 23.9 to 7; laser, 18.6 to 7.1).

Gilling *et al.*[173]

This randomised study assessed 86 men. Average operating times were 65 minutes for laser treatment and 49 minutes for TURP. Blood loss was greater after TURP, and hospital stays were longer.

Kitagawa *et al.*[174]

This small randomised study of 20 men treated by TURP and laser is only available in abstract form. Similar results were found with respect to changes in symptom scores (19.6 to 3.6) and flow rates (6.1 ml/s to 21.5 ml/s) after laser compared with TURP (20.4 to 3.7 and 6.7 ml/s to 21.5 ml/s). Both studies have shown that holmium laser treatment takes 20 minutes longer on average than TURP, but results in shorter stays and less blood loss (*see* Tables 19 to 23).

Transurethral ultrasound-guided laser prostatectomy (TULIP)

Schulze *et al.*[190]

In a trial comparing TULIP with TURP, 41 patients were randomised and enrolled, though the method of randomisation is not reported. Baseline characteristics of the groups were similar. Laser treatment was a significantly shorter (by 20 minutes) procedure than TURP. The TULIP ultrasound transducer is coupled to an Nd:Yag laser (Intrasonics Inc., Burlington, MA, USA) and power is delivered at a setting of 30–40 W. With ultrasound visualisation, laser passes are initiated at a pull rate of 1 mm/s, with 8 to 10 laser passes being conducted per procedure. The patients were followed up for 1 year, and evaluated by symptom score, peak flow rate and post-void residual volume. The clinical results demonstrate substantial improvements in each of the parameters. However, those patients treated by TULIP lagged behind those treated by TURP in the length of time required to improve, and the improvements in TURP patients were slightly better. Owing to the small size of the trial, the lack of statistical significance is not reliable. There were slightly fewer complications in the TULIP group (10%), and one treatment failure (5%). Men treated by TURP had three complications (14%) and one treatment failure (5%). Sexual function was not assessed.

Transurethral incision of the prostate (TUIP)

Nielson *et al.*[192]

In this prospective randomised trial, 24 patients underwent TUIP and 25 patients were treated by TURP. The average age of patients receiving TURP was slightly greater than those treated by TUIP (73 vs. 69 years), but in other respects the two groups were similar. The TUIP group had three more patients with very large glands (> 50 g), while the TURP group had four more patients with very small glands (< 30 g). TUIP had a significantly shorter operation time than TURP, and also resulted in significantly less peri-operative bleeding and a smaller number of blood transfusions required. The catheterisation time and length of hospital stay were the same for both groups. The patients were followed for 12 months, after which time there were no significant differences between the two groups for peak flow rates. Complication rates were higher for TURP, and included incontinence (4%) and stricture (17%). Of those randomised to the TUIP group, 12.5% developed post-operative retention and were treated by TURP. Although the authors cite an 82% success rate for TUIP, their analysis of this group includes the three patients who underwent subsequent treatment by TURP (*see* Tables 24 and 25).

Christensen *et al.*[194]

In this randomised controlled trial of TUIP vs. TURP, 93 patients with prostates weighing less than 20 g were randomised to one of the two treatment arms. The method of randomisation is not stated. The patients were assessed by uroflowmetry and symptom scores and followed up for 2 years. At 3 months of follow-up the total symptom scores were the same for both TUIP ($n = 35$) and TURP ($n = 38$). This was an improvement from pre-operative scores of 16 for each group. Three years after intervention, however, total symptom scores for TURP remained at 4 whereas the scores for TUIP had risen to 8 ($p = 0.09$), although n for each group was lower at this stage (TUIP, $n = 9$; TURP, $n = 11$). In terms of individual-specific improvement, there was little difference between the groups 1 year post-operatively, with patients in both groups reporting around 75% improvements. However, by 2 years the symptomatic improvement in those treated by TUIP had fallen to 56%, whereas improvement in those treated by TURP remained higher at 76%. Due to the large range of variation in scores for both groups, however, this was not statistically significant.

There was a significant difference in peak flow rates between the groups, with those treated by TUIP demonstrating less improvement than those who were treated by TURP. However, when the flow rates were analysed in terms of individual-specific change, there was no statistically significant difference between the two groups.

There were significant differences between the TUIP and TURP groups for operating times, blood loss, catheter time and post-operative hospital stays, all in favour of TUIP. In this study the operating time for TUIP was less than half that for TURP, and blood loss was only 20% of that for TURP.

Dorflinger *et al.*[195]

Thirty-eight patients were included in this study comparing the effectiveness of TUIP with that of TURP. Eligibility criteria included a prostate weighing less than 20 g. Baseline parameters were broadly similar between the two groups. However, the group that underwent TURP had a slightly higher symptom score than those who underwent TUIP (17 vs. 15), although this was not significant. There was a significant difference in the pre-operative frequency of micturition between the TURP and TUIP groups (14% and 29%, respectively). There were statistically significant differences in the surgical parameters, including operation time, which for the TUIP process was half of the mean time for TURP. Bleeding during surgery was also less for TUIP, and no TUIP patients ($n = 17$) required blood transfusions, compared to 19% of TURP patients ($n = 21$).

Complications for patients treated by TUIP included urinary retention in 12%, which was resolved by TURP. One patient (5%) in the TURP group developed retention, but there were no differences in incidence of treatment failures between the two groups. Patients were only followed up for 3 months. However, at the end of this period total symptom scores and peak flow rates had improved significantly for patients treated by either procedure.

Dorflinger *et al.*[196]

Thirty-one patients were randomised to be treated by TURP and 29 by TUIP. Pre-operative parameters for the two groups were similar. However, there were statistically significant differences between the groups, including length of operation and blood loss, both of which were lower for patients undergoing TUIP. Thirteen per cent of patients in the TURP group required blood transfusions compared with none in the TUIP group. However, this was not statistically significant. Complications reported included one patient (3%) receiving TURP who developed a urethral stricture. This compared well with the TUIP group, which reported eight treatment failures within the first year after surgery. Despite this, at the 3- and 12-month follow-up assessments both TUIP and TURP groups reported significantly improved symptom scores and peak flow rates. Men treated by TURP demonstrated significantly better improvements in peak flow rates and voided volume compared with those treated by TUIP, and subjective evaluation of the procedures gave improvements of 92% and 95% for TURP and TUIP, respectively, at both 3- and 12-month follow-ups. Four men (17%) who underwent TURP felt that their potency had worsened as a result of the operation, compared with 5% of TUIP patients, but these results were not significantly different. The number of patients who suffered from retrograde ejaculation after TURP (50%) was significantly greater than the number that suffered from retrograde ejaculation as a result of TUIP (5%).

Larsen *et al.*[197]

Thirty-seven patients with BPH were randomised to undergo TURP ($n = 18$) or TUIP ($n = 19$). The method of randomisation was not reported. Patients were assessed by uroflowmetry and symptom scores (Madsen and Iversen), and were followed up for 12 months.

The baseline characteristics of both groups were similar. Results at 12 months showed a statistically significant decrease in symptom scores as a result of both TUIP and TURP. Peak flow rates significantly increased after treatment by TURP and TUIP. However, the increase was greater for TURP than for TUIP. Of the men undergoing TUIP, 28% developed retrograde ejaculation compared to 100% of those being treated by TURP. For TUIP, catheterisation time and hospital stay were significantly shorter, although no information about the length of operation or blood loss was given. One patient in the TUIP group was readmitted to hospital with haematuria, which resolved spontaneously.

Riehmann *et al.*[198]

In one of the largest studies included here, 120 patients were randomised to receive either TURP or TUIP. Patients were evaluated by uroflowmetry and symptom scores (Madsen) and were followed up for 6 years. The method of randomisation was not reported. Total symptom scores decreased significantly after both TUIP ($n = 61$) and TURP ($n = 56$). There were no significant differences between the two groups, although TURP resulted in significantly higher peak flow rates than TUIP. Despite the randomisation process, patients in the TURP group had significantly higher pre-operative as well as post-operative flow rates. Of the patients in the TUIP group, 23% received additional treatment for BOO. This compared with 16% of TURP patients who required treatment other than TURP for infra-vesical obstruction. There was, however, no significant difference between the two groups in the numbers of patients who required additional treatment. Other measurements favoured TUIP over TURP, with significant decreases in operating time, blood loss, catheter time and hospital stay compared with TURP. Of the patients who were treated by TURP, 68% reported retrograde ejaculation compared with 35% of patients who were treated by TUIP. This difference was statistically significant. One patient died 90 days after TURP.

Soonawalla *et al.*[199]

In this trial, 220 men were randomised in equal numbers to be treated by TURP or TUIP. The method of randomisation was not reported. The duration of the operation, number of patients requiring blood transfusion, and duration of catheterisation and hospitalisation were all lower for TUIP than for TURP. However, it was not clear whether these differences were significant. The duration of surgery for TUIP ranged from 10 to 40 minutes (mean = 20.4) and for TURP it ranged from 30 to 95 minutes (mean = 59.2). None of the patients treated by TUIP, but 38 patients (35%) who received TURP, required blood transfusions during the procedure. All patients were followed up for at least 3 months. About 70 men in each group were followed for 1 year and about 20 men were followed for 2 years. At 3 months, peak flow rates in both groups had increased substantially, and this rise was maintained in patients followed up for 2 years. Of the patients who were treated by TUIP, 95.5% were satisfied with the outcome compared with 90% of patients who were treated by TURP. Serious complications (TUR syndrome or haemorrhage) were found more frequently in patients who had received TURP than in those who received TUIP. However, more patients in the TUIP group (6%) than in the TURP group (4%) failed to void following surgery.

Ttransurethral electrovaporisation of the prostate (TUEVP)

Patel *et al.*[200]

In one small randomised trial, 38 men were studied. Marked improvements were shown after TURP and vaporisation. No significant differences in outcome were found, but catheter time (48 vs. 23 hours) and hospital stay (2.5 vs. 1.2 days) were shorter after vaporisation. Complications included secondary bleeding

(3/21 after TURP and 1/17 after TUEVAP), stress incontinence (1/17 after TUEVAP) and ejaculatory dysfunction (5 new cases after TURP and 2 new cases after TUEVAP).

Standard TURP and 'minimal' TURP

Aagard *et al.*[207]

Conventional TURP was compared with minimal transurethral resection of the prostate (M-TURP) in 167 patients with BPH. The patients were randomised to the two treatment groups, although the method of randomisation was not reported. Follow-up analysis of symptoms and uroflowmetry were carried out at 6 and 12 months. Of 83 patients who underwent TURP and 84 who received MTURP, 33 and 29 patients, respectively, were available for further examination at 10 years. Nineteen patients who had had repeat operations in the interim period were not included in this analysis. Ten-year follow up showed that obstructive and irritative symptom scores remained stable over the follow-up period with no significant differences between the two groups. However, there was an increased need for repeat surgery in those who were treated by M-TURP compared with the TURP group (23% vs. 7%), which was reflected in a decreased average weight of tissue resected by MTURP (8 g) and TURP (14 g). The incidence of urethral stricture was increased after TURP (14%) compared with MTURP.

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